My ENCOUNTERS WITH TWO NOBEL PRIZE LAURETTES PROFESSOR BARUCH BLUMBERG & SIR SYDNEY BRENNER

DISCOVERER OF HUMAN HEPATITIS B VIRUS.(BLUMBERG) & Molecular studies on genetic regulation of Organ development and programming( SYDNEY BRENNER)

Background . BLUMBERG’S DISCOVERY

Discovery of Hepatitis B virus.

In 1965 , just as I was having my Cambridge University Final M. B exams, we learnt of the exciting discovery of the Australian antigen (which was associated with infectious jaundice) by Professor Baruch Blumberg and his team from Fox Chase Cancer Institute , Philadelphia, Pa, USA. The first published picture of that exciting discovery of the precipitin reaction between the Australia antigen and the antibody against it, was in the Journal of the American Association , by Blumberg, Alter and Visnich . This antigen was later found in dialysis patients, leukemia, multiple transfused persons, and many with acute and chronic liver diseases, including liver cancer. Liver Cancer was then one of the top three cancers in the Asia Pacific Region and the eighth in the world .

Picture: top well contains a leukemia patient’s serum, bottom well contains the sera of a multiple transfused patient, with hemophilia. The central line shows the combination of the Australia antigen and the antibody ( original picture, courtesy of Professor Baruch Blumberg 2011)
This virus, later called Hepatitis B, by the World Health Organization in 1973, was a human DNA virus, and transmitted by parenteral routes, such as needle stick infections, blood, saliva and sexually. In contrast the hepatitis A, a RNA virus, and was passed by eating virus contaminated food and water.

**Pioneer HB Vaccine**

In 1972, Blumberg and his team made the prototype vaccine, and soon patented it. But, Fox Chase Cancer Institute not was set up to manufacture it, and he sort the aid of the US manufacturer of vaccines, Merck & Co. At that time, the knowledge of hepatitis infection was in its infancy, being known for its acute illness, and seen in war torn conditions and not of chronicity. However Dr. Saul Krugman, a Pediatrician from New York, using a boiled serum from hepatitis infected cases showed that he could protect children entering a mentally retarded home of Down’s syndrome. Here the incidence of infectious jaundice was high. In 1971 a licensing agreement was signed up with a US manufacturer Merck & Co. Because much of the research had been US tax payers money the vaccine knowhow was not taken overseas. Dr. Maurice Hillman, a senior Executive, and Vice president of the Company was the most experienced person in making vaccines. He was put in charge of the project.

**My contribution to the HB Vaccine project**

In 1975, after completing Cambridge University post graduate M. D( Doctor of Medicine) in Cancer Immunology, I returned to Singapore, and was invited to set up a research laboratory and conduct research on liver cancer by the three doyens in local medicine, Professor Seah Cheng Seang, Professor Khoo Oon Teik, and Professor K. Shanmuratnam. Liver Cancer was then the leading Cancer cause of death and incidence in the country.

My team and I carried out clinical, basic, and epidemiological research, and by 1982, knew that HBV was a chronic disease, and closely implicated as a causative agent for the acute, chronic liver diseases and liver cancer, not only in Singapore but in the whole Asia Pacific region (see my book: 'A Cancer Vaccine that transformed Singapore and the World'. Published by Straits Times Press, 2011)
Because no commercial vaccines were available, and it was extremely costly, the Government decided to proceed to conduct research to manufacture the vaccine from the blood of human carriers. I was appointed the first Biomedical Principal Investigator for the research to manufacture the HB Vaccine, which we developed by 1985, to the laboratory level, but we could not transcend the jump to human usage, as we had no industrial Know-how of making vaccines for humans.

The World Health Organization gave us every help to enable us to developed into a vaccine Manufacture base for the region. In 1985, I was appointed by our Government and also by the International Agency for Research in Cancer/WHO to conduct a research to monitor the changing trends of Liver Cancer before and after Hepatitis B Vaccinations.

**Life saving vaccine**

We became the first country in the world on 1 October 1985 to launch the global vaccination of all our newborns, starting first in babies born to HBV positive mothers and all staff exposed to HBV. The Merck vaccine was chosen as the W.H.O vaccine for the study, for its known safety and efficacy.

We had teething problems in implementation, but these were iron out as parents and the public began to have more confidence in the vaccine as is saved the lives of their children and themselves.

Thereafter other countries within the region and elsewhere followed our method of introducing the HB Vaccine into the expanded vaccinations for babies.

WHO later adopted the vaccine for its global program to eradicate Hepatitis B and reduced liver cancer.

*Today many millions of children and adults' lives have been saved.*
Visit by Professor Baruch Blumberg to Singapore

On the 25 September 1992, Professor Blumberg visited Singapore as the Lee Kuan Yew Distinguished visitor, and visited our Ransome Research laboratory, Singapore General Hospital.

Picture: Professor Blumberg with the Director of Medical Services and Permanent Services, Ministry of Health, Dr. Kwa Soon Bee, at Headquarters of the Ministry of Health, College of Medicine, 24 September 1992

We shared with him the successful story of our nationwide HB Vaccination and how we monitored the outcome, epidemiologically and with the Cancer Registry. He learnt of our discoveries of several Vaccine escape mutants which were resistant to the natural and the vaccine antibody. He was glad to learn that we had patents for five of these products internationally, and congratulated us on this. He shared his experience of his own patenting problems. He saw, and was informed of our discovery of a new Hepatitis E infection locally.
Picture: Baruch Blumberg signing the Ransome Research Laboratory VIP visitors Book (24 September 1992)

Picture: Professor Blumberg with Ransome Research laboratory staff, Department of Clinical Research, Ministry of Health, who monitored the National Hepatitis B Vaccination program and some of whom were the first pioneers of Biomedical patterns from Singapore.

He shared many moments in a happy and cheerful dialogue session with our scientific research team involved in the monitoring of the vaccination project as well as in the patents.

Visit to Balliol College Oxford University

Professor Blumberg, Master of Balliol College, Oxford, invited me to visit his college the following year when I was up there for the Oon Family International Prize Award for Medicine by Cambridge University. We dined in Hall together with many senior fellows, and we met his wife Jean, who cycled in to meet us.

I sought his opinion whether the Hamster Ovarian Cell continuous transforming cell was safe to use, as a cell substrate for vaccine manufacture. He agreed with me that it was unsafe, because of its carcinogenic propensity. Later, back in Singapore, I would advise our Singapore Ministerial committee that this commercial vaccine was not safe for use in humans despite its promotion as a low cost and effective vaccine in poor vaccine responders.
A Cancer Vaccine proven on the 2 October 2010.

On the 2 October 2011, and on the 25th anniversary of the nationwide HB vaccination program, our Minister of Health, Mr. Khaw Boon Wan announced in our published book and on TV and the media, that Hepatitis B incidence had dropped from 9.1% (1975) to below 2.7% now, our Liver Cancer rates from 27:100,00 population (1978-1982) to 17.8:100,000(2002-2007) and there were no cases of young children under 15 years of age with acute hepatitis B. The vaccine was also proven safe with no long term side effects.


As a prime investigator for the vaccine project, I was glad that the vaccine was proven to be safe, effective, durable and prevented a major cancer of the world.

I sent this good news to Blumberg with my book. He was so delighted, that he sent me back his book "The hunt for the a killer virus. Hepatitis B. Winner of the Nobel Prize in Physiology or Medicine in 1976"
Picture: Book. Nobel Prize Nook by Nobel Prize Laureate, Professor Baruch Blumberg gave this to Professor Gabriel Oon on 21 February 2011, in recognition of work done for the Singapore and Global Hepatitis B Vaccination Program.

Picture: Blumberg's message to me, turns out to be his last.
"21 February 2011, Philadelphia, Pa, USA

"To my friend and colleague Gabriel Oon who has successfully moved forward the HB vaccination program in Singapore and achieved one of the earliest and most effective prevention programs worldwide.

With warm regards

Baruch Blumberg

I invited him to promote our book in the USA, but unfortunately on the 5 April 2011 while on a visit to a Presidential Council of Advisers meeting, he collapsed and passed away from a massive heart attack.

I lost a great friend and scientist.

Seeing God In Science

One day in Edinburgh, as a young doctor studying for my higher examinations, I placed the words of their famous poet, Robert Frost on the front of my table. It was to continue to inspire me to pursue on, no matter how great the difficulties.

" The Woods are lovely, dark and deep but I have promises to keep, and miles to go, before I sleep"

As I look back to to 46 years of Medicine, it has been a very long journey, from 1965 when I first graduated with my Cambridge MB.B. Chir, then, to obtaining my first postgraduate degree, a Diploma in Child Health, so that I could look after small very sick babies and older children; to passing the London Royal College of Physicians Membership of the Royal College of Medicine; and then to take up the new challenge to go into three years of basic and clinical research to study how to reject Cancer cells, and to understand how they developed.

It has been a long journey. On one part of that journey, I found the way to save so many lives all over the world.
My knowledge in Pediatrics had allowed me to look after sick babies and babies exposed to a new vaccine, and to know how to share the anxieties of parents.

**Fearlessness and trust in God**

To the many adults who feared receiving the first dose of an unknown vaccine, I showed by example to be the first to take the vaccine, trusting in God that he would protect me and keep me safe and help the program to spread all over the world.

The other, was as I began to see the light beyond the woods, I discovered in Science.. God ..my creator.

By asking basic simple scientific questions, how do the neutrons and atoms assemble together to form DNA and from them, the energy to make single cells life. Then how could these single cells live in a harmonious relationship without killing each other, or spreading like in cancer. Many times in quiet prayers and in conversation with God, I have his comforting presence, and knows that his response will always be for the Good of His human community.

**Sharing God with other scientists, religious and non religious**

Sometimes in answer to many doctors, scientists, friends and parents, who asked me " Why did you vaccinate your two children first?"

I replied .." I was first. then my two young children aged 8 and 6 years. I knew it was a safe vaccine, but I put my trust in God, and if God wanted this program to succeed then nothing will happen to all of us, from my family, my scientific staff to my medical colleagues, nurses, and the young babies.

**Another religious reason why the Yeast DNA recombinant vaccine had to be made.**

Professor Baruch Blumberg and Dr. Maurice Hillman were both Jews, but we both shared the same God of Abraham. I told them I was a Catholic, but many feared using the plasma vaccine, not from new vaccine fears but also from religious fears.
I told them that we had to make the yeast recombinant DNA Vaccine also for our non believers and for the Moslem brothers, also sons of Abraham, because some of them believed that the plasma vaccine could contain 'porcine material from the plasma donors' and not halal

Today the yeast recombinant DNA Vaccine is used all over the world, regardless of religion

In my dedication in my book, I wrote,

"Dedicated to all pioneers daring to venture into the unknown future, standing firm in their beliefs and trusting completely in God to keep them from the abyss of failure, so as to make the discoveries for the betterment of society."

2. Encounter with Professor Sir Sydney Brenner. Nobel laureate in Physiology and Medicine (2002) for "Genetic regulation of organ regulation and programming"

I was introduced to Sir Sydney Brenner by two persons. Professor Sir Keith Peters, Regius Professor of Physic of Cambridge University, and by the Singapore Government 's External Board of Advisors for Molecular Biology to the Institute of Molecular Biology in 2002.

I had known Professor Keith Peters, very much earlier when I had worked as a senior House Physician to Professor Colin Dollery, Clinical Pharmacologist at the Postgraduate School of Medicine, Hammersmith Hospital, London in 1970. He was then a Renal Physician.

Professor Sir Keith Peters, is on the Board of our Oon International Prize for Medicine (see Oon Khye Beng Oon International Prize for Medicine), and was also on the first external panel of experts advisors to the Singapore Government for Molecular and Cell Biology. He introduced me to Sir Sydney Brenner when they both came to Singapore.

Sir Sydney Brenner visited our Ransome Research Laboratory in 2002, and praised me for our molecular virology of Hepatitis B viruses, which had led us to have five industrial patents, the first biomedical patent in Singapore. At that time I was also the Principal Investigator for the WHO Hepatitis B Vaccination program which was started on a National scale for all our newborns in Singapore. This was the first country in the world to initiate global immunization against Hepatitis B.
Sir Sydney Brenner made his most famous remark to our then Prime Minister Lee Kuan Yew, when the latter objected to starting an institute to do research. Brenner said "If you want to be a technician, then you will forever be a technician. The future is research and development".

The notion of a research Institute was strongly backed by the then Minister of Education, Mr. Goh Keng Swee (see excerpts on page 59. A Cancer Vaccine that transformed Singapore and the World" published by Straits Times press Ltd. 2 October 2010., and in "My Medical research in website: Gabrieloon.com)

![Photo: Professor Sir Sydney Brenner, of the Medical Research Council Institute at the Department of Medicine, Cambridge University, Cambridge.](image)

I was greatly inspired that in my brief life time of Cancer Research, I had met two such great men. They were humble, eager for knowledge, and questioned me about our projects.

***I reflected " Some Men are born to be great, others earn it, yet others are conferred on them by their contribution to the numerous lives that they had saved "
