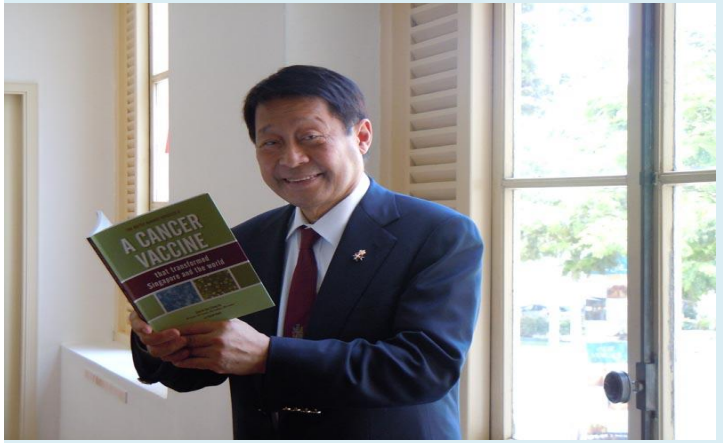
The Hepatitis B Vaccine Project 34 Years Later…

Did it achieve its objectives?

Dr Gabriel Oon Chong Jin

MD (Cantab), FRCP(London), FAM (Singapore), DCH(London)

1975-1986	Then Associate Professor of Medicine, Consultant Physician (Head, Division of Oncology & Immunology) University of Medicine, SGH
1978	Founder President Singapore Society of Oncology & Oncology Research in Singapore
1982-1987	Principal Investigator, Ministry of Trade and Industry: Research and Development of a Hepatitis B vaccine for human use
1983-1986	First Chairman: Ministry of Health Scientific & Advisory Committee on Hepatitis and Related disorders
1983-current	Principal Investigator, International Agency for Research in Cancer, W.H.O “Outcome of Liver Cancer before and after hepatitis B Vaccines.
1983-2005	Director, WHO Collaborating Center for Hepatitis B Vaccines
1985-2005	Consultant and Advisor, World Health Organization for Biological Standards, Hepatitis Vaccines and Cancer Prevention



Dr Gabriel Oon Chong Jin

Medical Oncologist & Physician

Mount Elizabeth Hospital

MA., M.D Cantab., FRCP (London), FAMS, DCH (London)

“ The benefits of cancer prevention, unlike advances in cancer treatment, are mostly invisible to the public at large. At the same time it is prevention that most effectively relieves the disease on individuals, their family and friends and on society in general. The world needs people and their stories that champion cancer prevention. ”

Christopher P Wild, PhD

Director, International Agency for Research on Cancer (IARC)
Lyon, France

Nobel Prize Discovery for Structure of DNA 1962

Watson, Crick and Wilkins

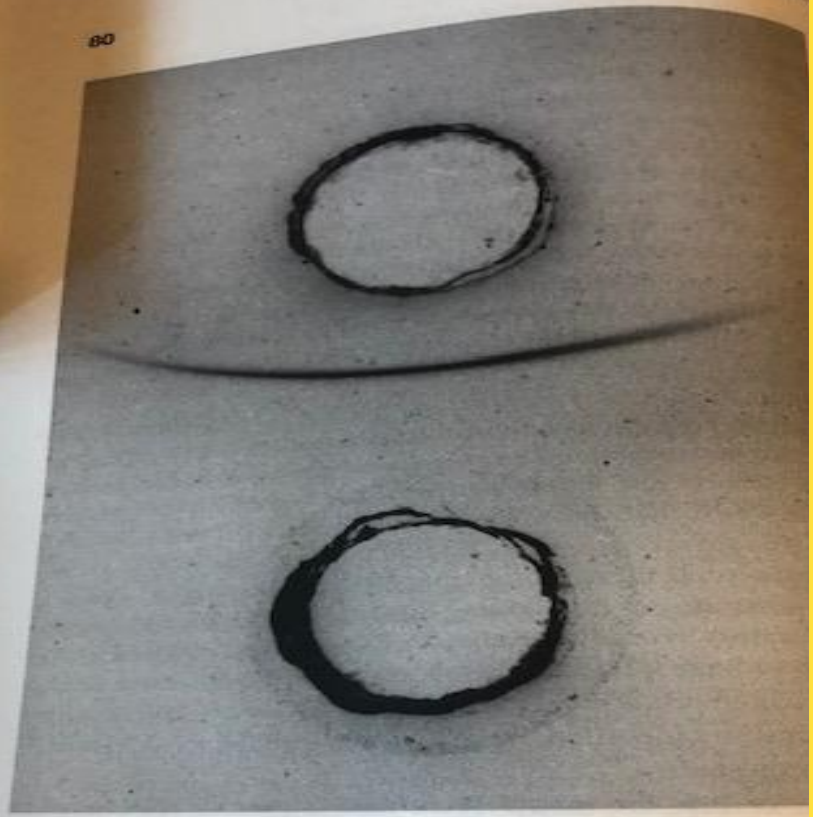


Fig. 1. The first published image of the precipitin reaction in agar gel be
antigen and the antibody against it. The precipitin is the combination of
antibody that forms a visible band in the gel. The top well contains the s
patient with leukemia who is a carrier of Australia antigen. The bottom v
serum from a hemophilia patient who has received many blood transfus
contains antibody against Australia antigen. (Blumberg, Alter, and Visni
the American Medical Association 191 [1965]: 542.)

The hunt for a killer virus

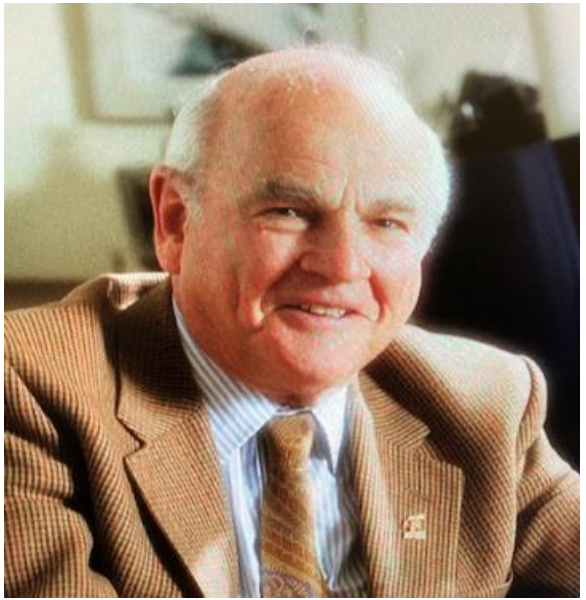
Hepatitis B

Baruch S. Blumberg

Winner of the Nobel Prize in Physiology or Medicine

Discoverer of HBV

Prof Baruch Blumberg , USA
Nobel Prize, 1976



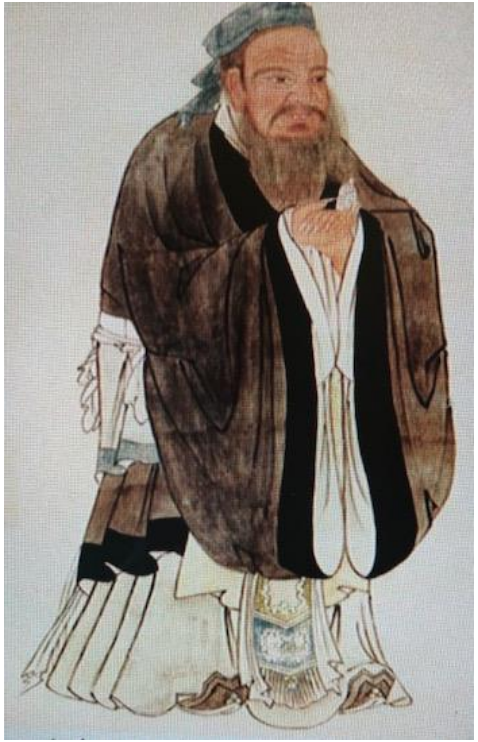
Background

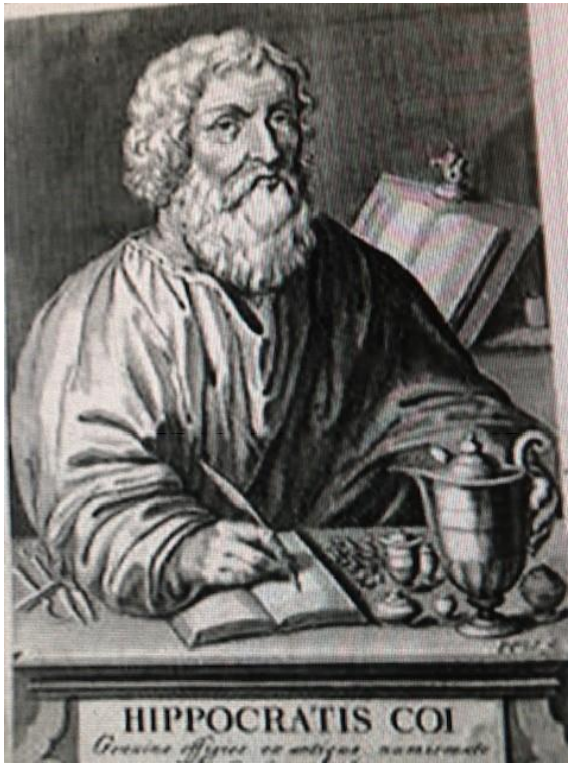
Sir Gordon Ransome & Prof Seah Cheng Siang

- 1973 - Cambridge M.D. Invited by three eminent persons:
  - Professor Seah Cheng Siang (Singapore)
  - Professor David Todd (Queen Mary Hospital, Hong Kong)
  - Mr. Sung Chi Kuan (Chinese Ambassador to United Kingdom)
- “Go back East and help your people”
- 1975 - Appointed Junior lecturer University of Singapore.
- Asked by three eminent Professor of Medicine:
  - Professors Khoo Oon Teik (Head, University Department of Medicine),
  - Professor Seah Cheng Siang (Government department of Medicine III @ Singapore General Hospital) &
  - Professor Shanmugaratnam , Professor of Pathology and head of Singapore Cancer Registry (formed by IARC)
- Conduct Liver Cancer Research
  - Top killer and No.1 Cancer in Singapore, the Asia Pacific Region and sixth in the world.
  - Given a small attic laboratory and called it the Ransome Research Laboratory.
  - No funds from university.
  - Lee Foundation S$10,000 enabled employment of one PH.D scientist and one technician.
  - Later Shaw Foundation and Turf Club funded most of research

History

HBV – Mysterious Killer of Ancient Times



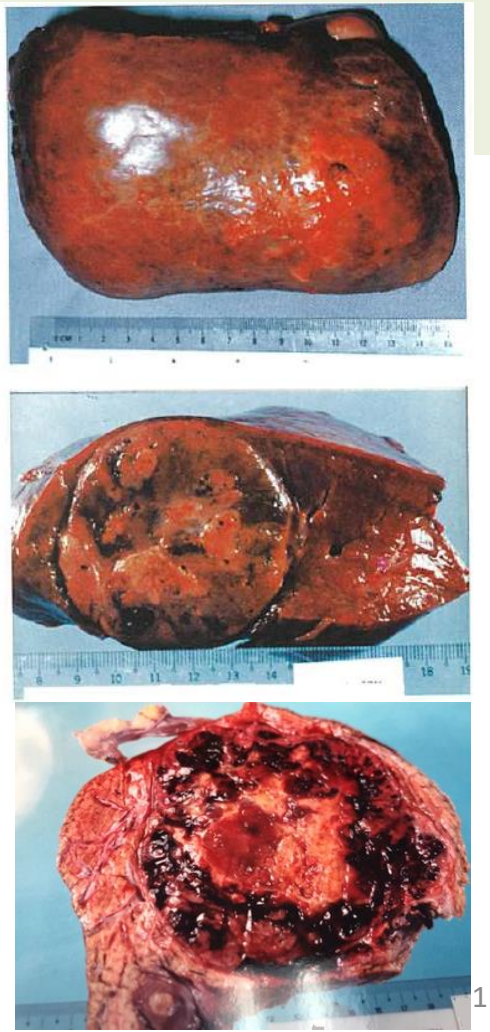


← Nazi medical experiments at the Buchenwald concentration camp in World War II

← A “death house” in Sago Lane, Chinatown, Singapore

Early Studies

1. Pilot Trial of immunotherapy using families with AntiHBs to treat carriers who were HBsAg positive. Ineffective.
2. Many recurrences of Liver Cancer after resection. 80% in first year.
3. HBV is main cause of many deaths from acute liver failure, bleeding varices, and liver cancer.
4. HBV transmissions from HBV positive mother to child, intrafamily, sexual routes, unclean instrumental procedures (dentistry, surgery, needles,) acupuncture, mosquitoes, bed bugs, barbers shavers, blood transfusions and blood products, wounds from HBV positive persons.
5. Aflatoxin in food stuffs (exposed rice, sauce, peanuts etc.) and ingested in 4% of a random population of volunteer staff and medical students. Led to legislation and banning of imported food to have less than 1 part per billion of Aflatoxin.



Interpreting Hepatitis B Markers & Management

	Normal	Vaccinated	Just Infected (within 24 hrs)	Chronic
HBsAg	0	0	Positive	Pos/Neg
AntiHBs	0	Positive	0	Neg/Pos
AntiHBcIgG (HBV in liver)	0	0	Positive	Positive
HBVDNA	0	0	Positive	Pos/Neg
Treatment :	**Vaccine**	**0**	**HBIG & Vaccine**	**aIFN & antivirals**

Hep B Serological Markers in HCC, other Cancers and Normal Population

Table VI. Hepatitis B serological markers in primary hepatocellular carcinoma and age-matched neoplastics and controls

	Total	HBsAg	AntiHBc	AntiHBs	'e' Ag
1. Primary Hepatocellular Carcinoma Mean Age 54 yrs ± 11.7	150	102/150 (68%)	69/74 (93%)	12/28 (43%)	6/39 (15%)
2. Other Solid Tumours (Breast, Stomach, Colon, Prostate etc) Mean Age 55 yrs ± 4	47	4/47 (9%)	39/47 (75%)		
3. Normal Adult Population Mean Age 54 yrs ± 5	100	10/100 (10%)	60/98 (61%)	11/16 (69%)	

HBV Markers with Different Ages

Table II. Differences in Hepatitis B markers between males and females

Age in Years	Sex	HBsAg			AntiHBc			AntiHBs		
		No. of children tested	No. of children positive	Percentage	No. of children tested	No. of chilren positive	Percentage	No. of children tested	No. of children positive	Percentage
< 1	M	110	13	11.8	100	26	26.0	109	25	22.9
	F	70	3	4.3	58	22	37.9	69	26	37.7
1- < 3	M	48	7	14.6	46	10	21.7	48	7	14.6
	F	30	2	6.7	30	4	13.3	30	4	13.3
3- < 6	M	34	5	14.7	33	8	24.2	34	4	11.8
	F	28	0	0	28	1	3.6	28	1	3.6
6- < 9	M	37	8	21.6	36	12	33.3	36	7	19.4
	F	19	1	5.3	19	5	26.3	19	0	0
9- < 12	M	37	7	18.9	35	13	37.1	37	6	16.2
	F	18	1	5.6	18	4	22.2	18	3	16.7
TOTAL	M	266	40	15.0	250	69	27.6	264	49	18.6
	F	165	7	4.2	153	36	23.5	164	34	20.7

Hepatitis B Seroprevalence in Singapore Population 1976-82 (WHO Meeting , Athens 1982)

Table IV. Immune status of various normal populations to Hepatitis in Singapore

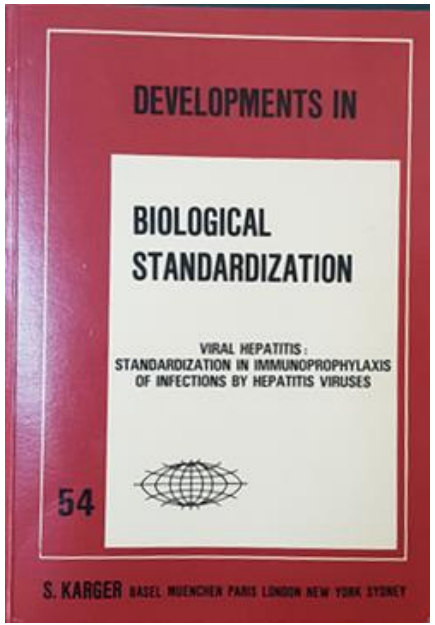
AGE GROUP BIRTH TO 12 YEARS	TOTAL	POSITIVE HBsHg	POSITIVE ANTI HBc	POSITIVE ANTI HBs
MALES 1-12 YEARS	266	40/266(15%)	69/250(27.6%)	49/264(19%)
FEMALES 1-12 YEARS	165	7/165(4%)	36/153(24%)	34/164(21%)
AGE GROUP (20 - 29 YEARS)				
MALES :	58	2/53 (4%)	8/57(14%)	3/47(6%)
FEMALES :	192	8/190(4%)	39/192(20%)	32/172(19%)
AGE GROUP (30 - 39 YEARS)				
MALES :	36	3/34 (9%)	12/36(33%)	9/30(30%)
FEMALES :	109	3/108(3%)	46/109(42%)	35/89(39%)
AGE GROUP (40 - 49 YEARS)				
MALES :	26	2/25(8%)	15/26(58%)	14/23(61%)
FEMALES :	33	1/33(3%)	15/33(46%)	12/25(48%)

HBV Infection in Different Ages

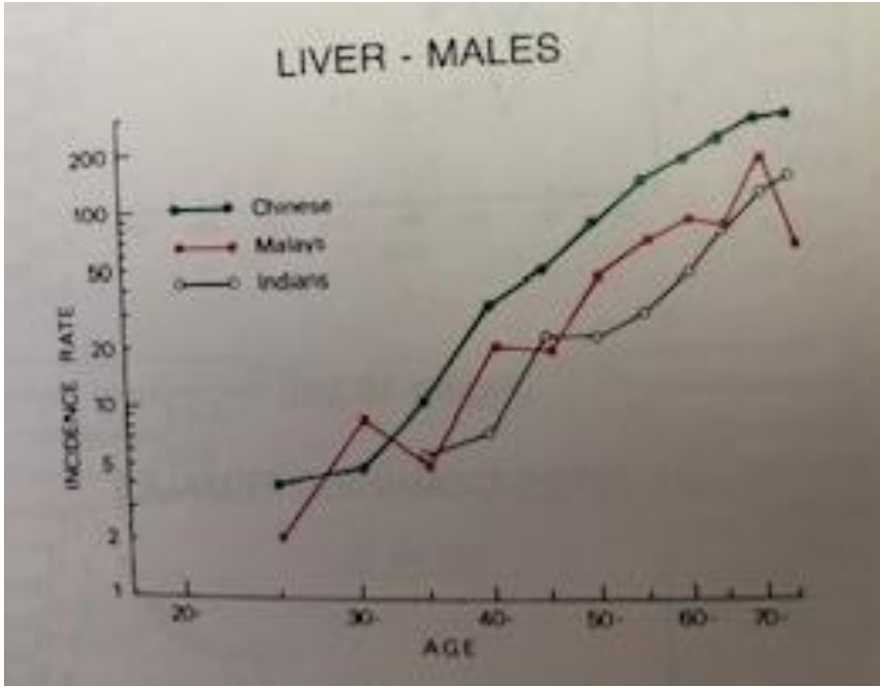
- 1975 - 1983.
  - 430 patients from birth to 76yrs
  - Epidemiology studies study extent of HBV using HBsAg, antiHBcIgG, antiHBs)
  - Aflatoxin identified with IARC/WHO led to legislation banning importation in food

- HBsAg 11% in population

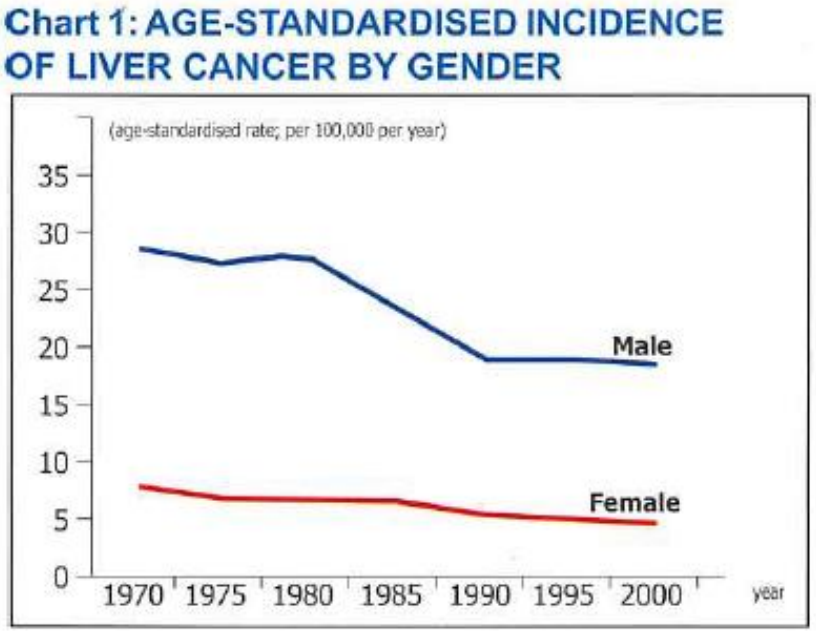
- AntiHBc IgG
  @ birth 5%
  @ 20 years 20%
  @ 40 years 50%
  @ 60 years 70%



Liver Cancer



Liver Cancer 1968 - 1977



Objectives of Hepatitis B Vaccine Project

1. Obtain a safe and effective vaccine against HBV
2. Eliminate liver cancer
3. Make affordable vaccine to protect our population and the world
4. Make absolute safe vaccines
5. Develop industrial knowhow and higher quality industries in Singapore

BUSINESS TIM

M.C. (P) No. 66/1/84

WEDNESDAY, JANUARY 25, 1984

Hepatitis vaccine plant is fifth Asean project

By LOH HUI YIN

The Making of Hepatitis B Vaccine

WHO THIRD TASK FORCE MEETING ON HEPATITIS B : 29 SEP 1985 : NAGASAKI CHUO NATIONAL HOSPITAL

WHO Meeting in Geneva 1982

IARC Contract to Study Outcome of Liver Cancer before and after HB Vaccine

WORLD HEALTH ORGANIZATION

ORGANISATION MONDIALE DE LA SANTÉ

CENTRE INTERNATIONAL DE RECHERCHE SUR LE CANCER

INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

A G R E E M E N T

BETWEEN The University Department of Medicine, Singapore General Hospital, Singapore, hereafter known as the "Department"

AND The International Agency for Research on Cancer, Lyon, France, hereafter known as the "IARC"

The IARC agrees to provide to the Department a sum equivalent to US$ 22 550 (TWENTY TWO THOUSAND FIVE HUNDRED FIFTY US DOLLARS)

for the period commencing : 15 March 1983
to : 30 November 1983

to monitor liver cancer trends before and after the introduction of a Hepatitis B vaccine. The work to be undertaken is summarized in the attached "Statement on Research or Other Technical Services to be Rendered" which is an integral part of this Agreement.

The Department accepts the "General Conditions" attached, in so far as they may be applicable, which are also an integral part of this Agreement.

On signature of this Agreement a sum equivalent to US$ 22 550 (TWENTY TWO THOUSAND FIVE HUNDRED FIFTY US DOLLARS) will be made available to the Department.

ON BEHALF OF THE IARC

Signature

Name : L. Tomatis, M.D.
Director

Date 11/7/83

ON BEHALF OF THE DEPARTMENT

Signature

Name : PROF WONG POI KWONG
Head, Dept of Medicine

Date 12/4/83

WHO Warnings of Vaccine Disasters

- *Lubeck, Germany 1959.
- 240 vaccinated accidentally with living BCG vaccine. 70 died of disseminated TB
- *Cutter accident. five western US states , USA 1955.
- 200,000 children infected with life polio vaccine . 70,000 paralysed. 10 died.

Early HB Manufacturers 1983-5

Method : By protein fractionation of infected HBV positive blood from doors.

- MSD(USA) three stage inactivation (Urea, Pepsin, Formalin). phase 1 studies in USA
- Pasteur (France) one stage inactivation(Formalin) phase 2 studies in Gambia with IARC/WHO
- Brummelhuis (Nederlands BTS). HBV blood for vaccine (heat inactivation alone) Phase 1.
- Singapore (purification stage)
- Green cross (Japan & Korea) purification stage.

1985 Onwards

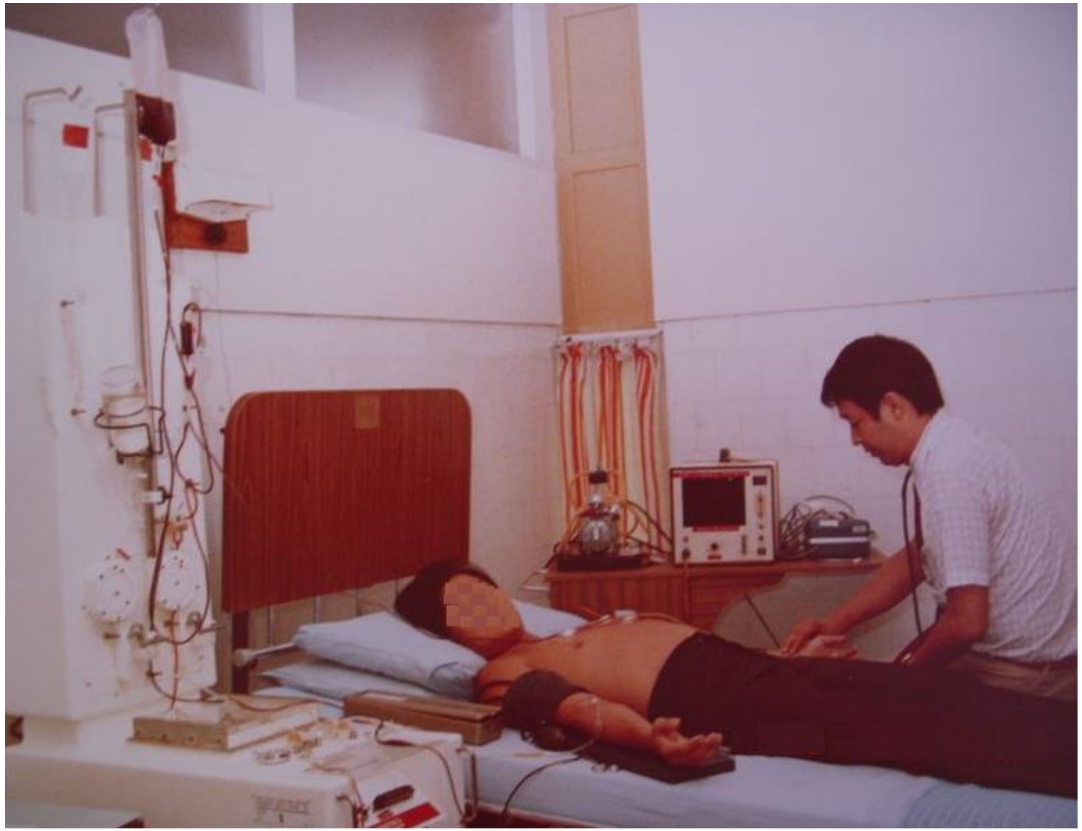
- MSD(USA) with Singapore: Yeast recombinant HB Vaccine (formalin inactivation) Phase 2 to field use thereafter
- 2005 GlaxoSmithKline in Singapore: Yeast recombinant HB Vaccine (formalin inactivation) . field use to this day

In Research

- Amgen(USA)
- MSD, (USA)
- SKB (UK) later as Glaxosmithkline yeast recombinant HB vaccine
- Singapore
- others

Haemonetics Blood Cell Separator

Used for the First Time in Singapore in 1993



Earliest Recipients

First children in Singapore to receive the plasma-derived Hep B vaccine.

- As early as 1983, Singapore received 20 vials of Hep B vaccines
- Researchers sill working to dispel fears about the safety of the vaccine
- Vaccine was felt to be 100% safe, but Mr Lee Kuan Yew wanted it made **300%** safe!

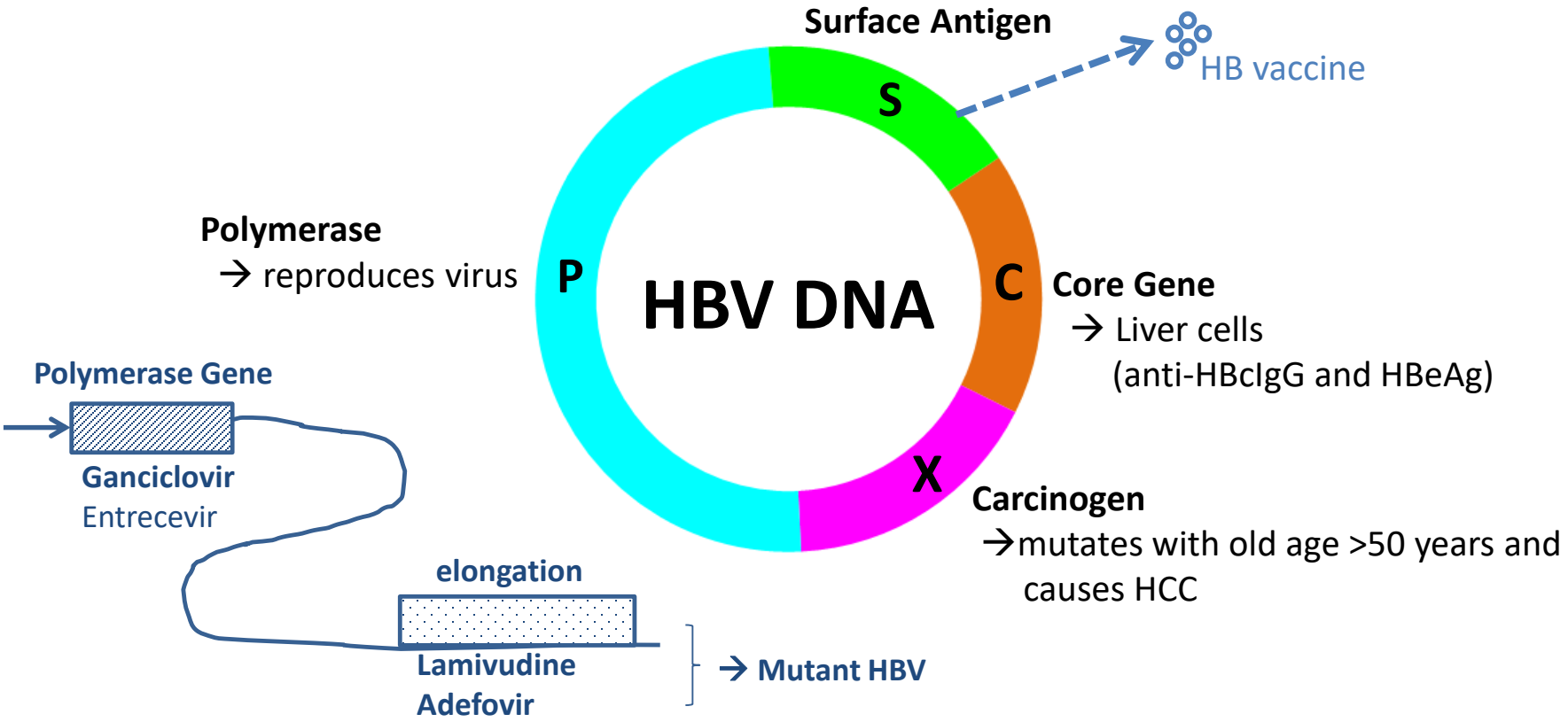
1983 – 1987 Fears of Hepatitis B Vaccine

- HBsAg particle would produce liver cancer
- Unknown microorganisms in vaccine
- Inadequate inactivation of unknown AIDs agent /& others
- Mad cow disease, early dementia
- Autoimmune diseases (blood product)
- Neurological diseases (HBsAg near similarity to myelin basic protein)
- Vaccine manufacture quality control safety

1983 – 1987 Overcoming Fears of Vaccines

- One of eight WHO Expert Collaborating Centres for HB Vaccine
- Use of only WHO approved/recognised vaccine
- Top local scientific experts on the MOH Scientific & Advisory Committee
- Use judiciously first-generation vaccine on the highest risk first
- Set up regulation for importation of medicines, vaccines, etc

Cross Section of Hep B Viruses (magnified)



Plasma Escape Mutants HBV “S” Antigen

- PRESENT in some plasma vaccinees.
- GYCLINE TO ARGININE 145 ady strain (Singapore strain)
- METHIONINE TO THREONINE 133 ady strain (Oon strain)
- PRESENT IN SOME RECIPIENTS OF PEPSIN, UREA, AND FORMALIN INACTIVATION NOT BY FORMALIN ONLY.
- Features: HBsAg negative, high antiHBs, Positive aniHBcigG, HBVDNA positive (can be negative initially)
- AntiHBs, natural and vaccine do not neutralize/destroy mutant
- Mutants destroyed by antiviral agents
- NOT PRESENT in YEAST RECOMBINANT Vaccinees.

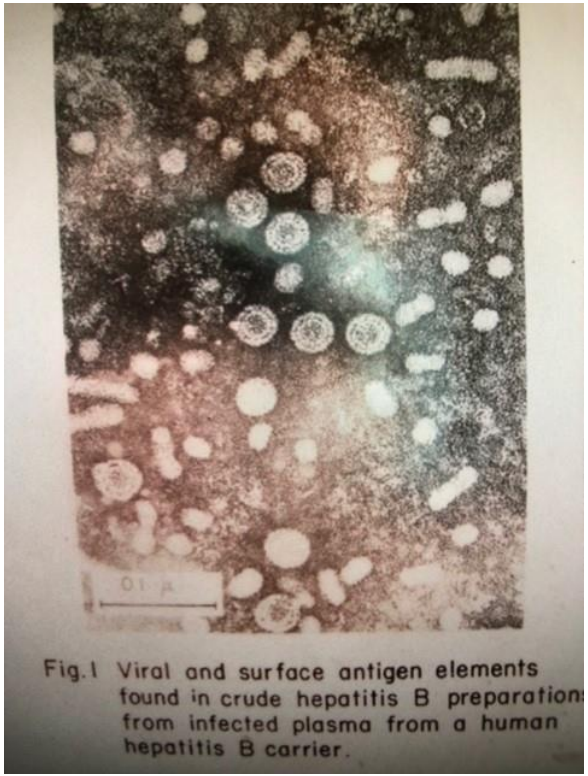


Fig.1 Viral and surface antigen elements found in crude hepatitis B preparations from infected plasma from a human hepatitis B carrier.

Innovation and Patents in HBV Vaccine Research

1. Maurice Hilleman (1969) MSD, USA. purification and three step inactivation with urea, formalin and pepsin.
2. Philip Maupas. A Goudeau. Processing from Plasma (1980)
3. Venezuela (Chiron). recombinant yeast vaccine (1986)

Oon C.J. Chen W.N et al, first five Singapore Biomedical industrial patents

4. Vaccine escape mutant 145 Glycine to Arginine. Singapore strain (1998)
5. Diagnostic assay (2001)
6. In vitro HBVDNA assay screening for inhibitors assay (2002)
7. Vaccine escape mutant 133 Methionine to Threonine (Oon Strain) (2004)
8. Detection of HBV surface mutants by specific application of Gene chips ((2004)

Ease, Difficulties and Dangers

A. BLOOD OF CARRIERS

Ease: Millions of HBV carriers, ready source

Requirements: Healthy, disease free, high titer HBsAg (usually from HBeAg and HBV DNA positive with HBsAg titer over 150ug/ml).

Dangers: human borne disease like HIV and others at molecular size transmitted to millions of recipients. Required intensive purification to have just pure HBsAg, and the product intensive sterilized by Urea, Pepsin and Formalin to kill the AIDS agent, all unknown pathogens, known and unknown.

Outcome:

- Used from 1983-5 in limited scale and trials until second generation HB Vaccines by genetic engineering arrived
- Vaccine escape HBV discovered by us in a few recipients, were not killed by Vaccine antibody and natural antibodies but by antiviral drugs . Became obsolete in 1987 and replaced by the yeast recombinant vaccine.

Ease, Difficulties and Dangers

B. EUKARYOYTES

like Saccharomyces cerevisiae (yeast). Single cell organism, with endoplasmic retinaculum, cell membrane, a nucleus. Present in protozoa, fungi, plants, moss arthropods and mammals

Outcome: Of all these eukaryotes tested only the Cerevisiae (yeast) was found to be safe for human. Chinese Hamster Ovarian not safe.

The yeast recombinant HB Vaccine was tested in trials in Singapore in 1985, found to fulfill WHO criteria, on safety and effectiveness and free of mutant HBV . It was adopted thereafter in Singapore from 1987 and is the standard vaccine used for the last 31 years. Since 2005, it is manufactured in Singapore by Glaxo Smith Kline, a World famous Vaccine and pharmaceutical company. MSD also made this vaccine, and we used it first , until 10 year contract expired . Today we use only the GSK yeast recombinant vaccine., as MSD declines world wide.

Ease, Difficulties and Dangers

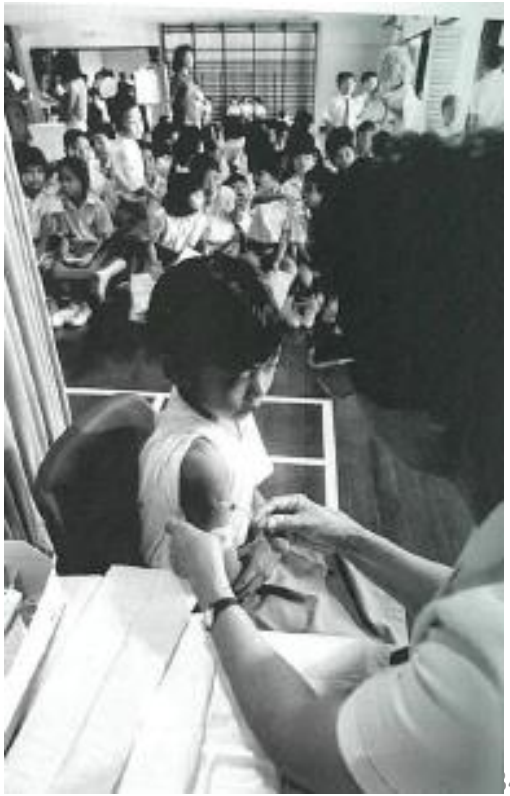
C. PROKARYOCYTES

From single cells with no nucleus. E.g Bacteria, actinomyces, cocci, vibrio.

Outcome: some done, but not safe.

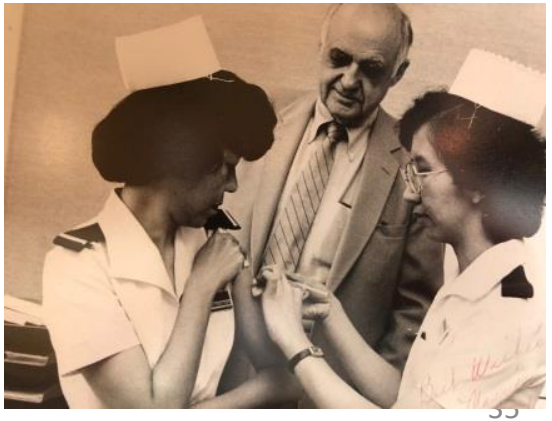
Singapore Programme Begins

- 1st October 1985. Launch of IARC/WHO Singapore HB Vaccination program, with MSD Plasma derived Vaccines (a WHO designated vaccine) to: babies born of HBV positive mums, extended to the population and other hospitals. GPs and clinics use vaccines.
- Drug licensing & prior approval of all medicines entering Singapore.
- 1st September 1987. Universal Vaccination of all new borns with the Yeast recombinant vaccine (MSD)
- Yeast vaccine only vaccine used in country from 1987 to even today 2018 (The Glaxo, Smith Kline) manufactured in Singapore since 2005



Early Programme

- 1978-82. Random Population Seroepidemiology studies completed.
- 1983. Pasteur vaccine for only ten.
  Director, Medical Services(MOH), Dr. Andrew Chew recommended Research team to take it as they were exposed to high risk of infected patients and handling HBV blood.
- Prof Oon first, then Dr S.E Aw followed by Miss Lim Gek Keow (Research technician) & the rest of the Research staff.
- 3 months later (more vaccines). Prof Oon's two sons, SL(8yrs), SF(6yrs) first children in this region to take it,
  followed by Prof Oon's wife Susie.
- Volunteer Healthcare staff, such as doctors, nurses, technicians, students, cleaners at the SGH
- Phase I vaccination of high risk HBV positive mother's babies at birth with MSD Plasma vaccine.



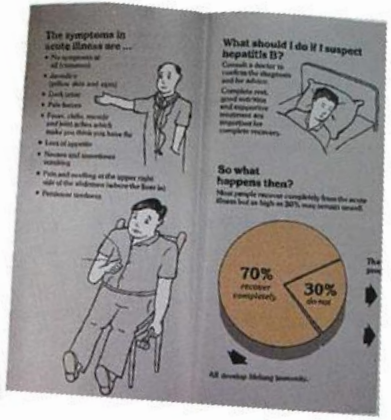
How Did Singapore Avert Disaster 1983 – 2000 & Murphy's Law ?

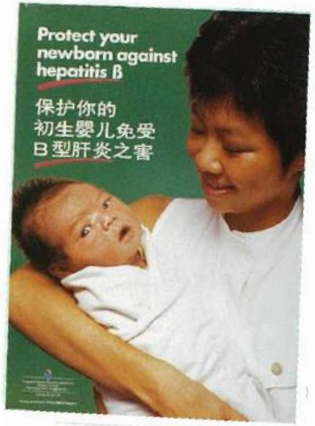
1. Chose at the beginning ,only WHO approved plasma based HB vaccine, regulated by FDA, and closely monitored by WHO experts
2. Avoiding unknown manufacturers, poor regulation , and unsafe procedures.
3. Use of disposable syringes and needles ,and Mediwabs before vaccination
4. Highest risk taking first voluntarily. (research staff, next SGH medical , nursing and dental staff, then medical students and newborns of carriers Mums or where there is HBV in family.
5. Stay linked to advanced new technology to make from non blood source
6. Discovery of the Saccromyces cerivisae (yeast) as effective promoter of the gene "S" of HBV to produce HB vaccine and use it
7. Not swayed by temptations of cheaper vaccines , with attached "goodies"
8. Stayed on course on a successful method.
9. Brought a top Vaccine manufacturer Glaxo Smith Kline (2005) to make HB vaccine and other vaccines for Singapore and the world.

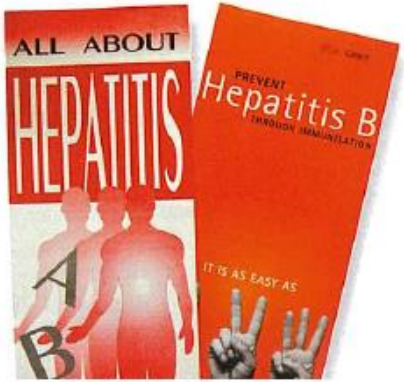
Yeast
Saccharomyces
Cerevisae
Recombinant
Vaccine

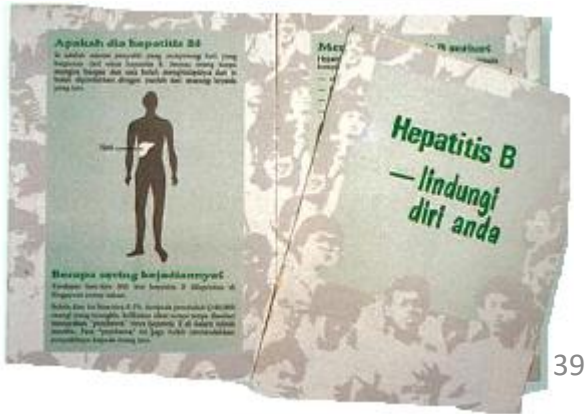
Education Changes & Industrial Transformation

Public Education Throughout the Years (1986-2010)





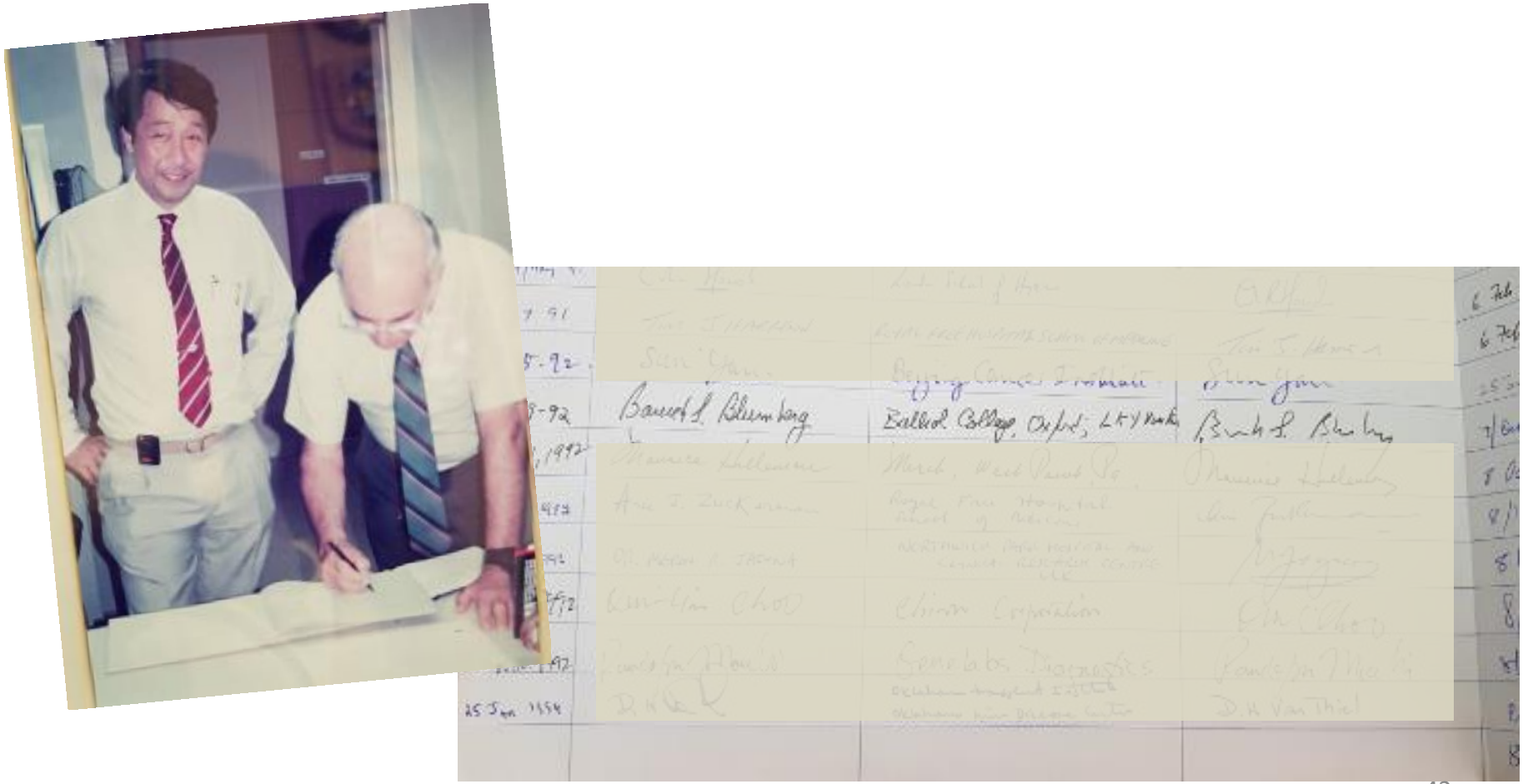




Start of Industrial Transformation - IMCB

Prof Blumberg in Ransome Liver Cancer Research Lab (SGH) on 24 Sept 1992

Left: Dr Oon Chong Jin, Prof Baruch Blumberg and Dr Kwa Soon Bee


Baruch S. Blumberg
Balliol College, Oxford, U.K.

25 and 34 Years Later

25 & 34 Years after Hepatitis B Vaccinations (MOH Data)

2013

- HBsAg prevalence (under 17 years). 0.3% ++
- HBsAg adults (>30yrs) 3.6%
- AntiHBcIgG Under 30 years. < 4.4%

  2008-2013 survey (Cutter J, Goh Kee Tai et al. Vaccine. 2013)

  ++ ASEAN Countries objective to achieve below 1% by 2010

2018

* AntiHBcIgG. < 40 yrs. Less Than 4%
* No sick children under age 17 years.
- No child under 17 years has HBV.

34 Years later 2018 – MOH HBV Status & Liver Cancer

- 100% coverage of all children at birth and under 20yrs old since 2001 (Medisafe & Edusafe respectively).
- No acute HBV under the age of 17 years old.
- Less than 4% antiHBcigG positive under the age of 40 years.
- No Liver Cancer under the age of 40 years.
- Liver Cancer prevalence decreased from 27.7 per 100,000 (1975-85) with 2.3 million population to **12.3 in 2018**.
- No females with liver cancer in the top 10 cancers in Singapore (Singapore Cancer Registry) Males No: 4 from No:1 (1975)
- Recombinant Yeast HB vaccine **safe**. No short term nor long term feared side effects.

Liver Cancer Trends in Singapore 1975-2018

(SINGAPORE CANCER REGISTRY. Formed by IARC/WHO in 1962 with the University Department of Pathology, National University of Singapore)

Primary Hepatocellular Carcinoma (HCC) forms 95% of Liver Cancers seen throughout time. The remainder are Cholangiocarcinoma

- **1978-1982. Liver Cancer rates. 27.7 per 100,000**
  - Majority was HCC. [It was No: 1 Cancer for Malays and in the country. Females were No:4]
  - AGE GROUPS. The incidence began from incidence of 2:100,000 in the age 20-29-year group climbing to a peak age group in the > 75 years. Males were 100: 100,000 and females 50: 100,000.
  - CHILDHOOD (less than20 years). There were no childhood Liver cancers below age of 20 years.
- **2002-2007. Overall rate was 17.8 per 100,000**
  - Incidence in females fell from 7.0 to 4.7 per 100,000
- **2010-2015. Overall Incidence 16: 100.000**
- **2016. Overall 16**
  - 16 Males 62: 100,00 (1,550 cases)
  - Females: 9 (< 500 cases)
- **2018. Overall**
  - 12.3 per 100,000

Were the Objectives Achieved?

34 years after Hepatitis B Vaccination (1985) & Research (1975)

Vaccine Objectives – Public Health & Industrial Know How

1. Available in abundance ✓
2. Low cost ✓
3. Absolute safety (short & long term) ✓
4. Vaccine manufacture disaster ✗
5. Vaccine administration failure and HBV infections ✗
6. Vaccine made in Singapore (to FDA, and WHO regulation) ✓
7. Vaccine know how technology transfer to Singapore ✓

Vaccine Objectives – Public Health & Industrial Know How

9. Achieve ASEAN Industrial Project Objectives ✓
   (Vaccines in all ASEAN countries, Hong Kong and the rest of the world)
10. Any feared diseases opportunistic infections by manufacturer ✗
11. Myelin degenerative disease ✗
12. Early dementia (Mad Cow disease) ✗
13. Liver Cancer from HBsAg of the vaccine ✗
14. Autoimmune diseases ✗

34 years after Hepatitis B Vaccination (1985) & Research (1975)

Vaccine Objectives – For HBV

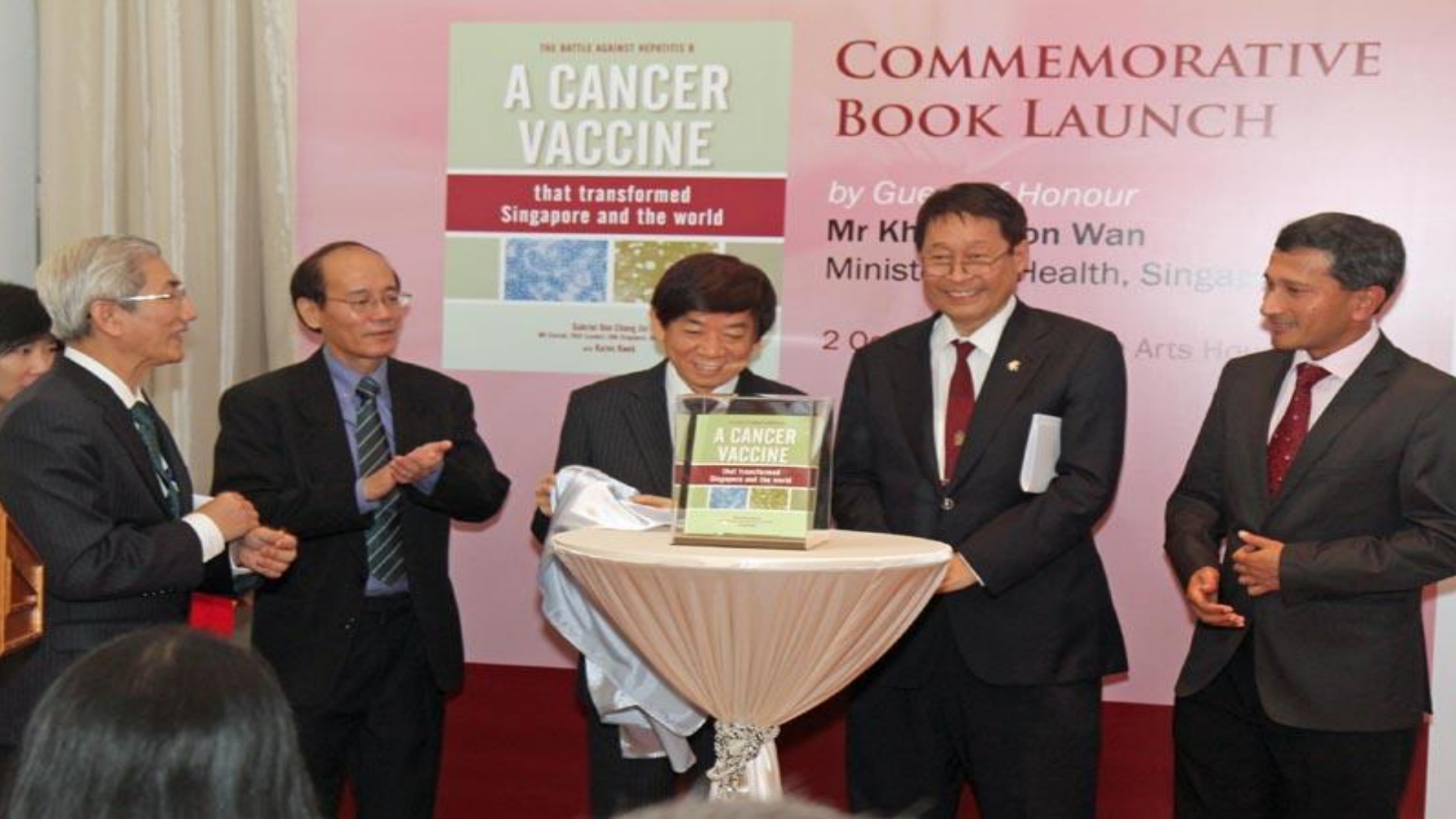
1. Elimination of HBV ✓
2. Elimination of HBV Cancer ✓
3. Healthy Vaccinated Children ✓
4. Longer living - 70.2 yrs (1975) to 82.6 yrs (2016) ✓

“Go Back & Help Your People in the East” ✓

3 Generations, all vaccinated

Other Spins Off

1. The stringent emphasis on control and prevention from: sexual transmission of diseases , blood transfusions , using only disposable needles & syringes (& not recycled) , now applies to control of all transmissible blood borne infections , like HCV, HIV.
2. Blood bank has now introduced nucleic acid testing (not CIE, rPHA ,etc.) for blood donations, making ours one of the safest blood supplies in the world.
3. Glaxo Smith Kline, a top vaccine manufacturer, with WHO & FDA qualities started manufacturing the yeast recombinant vaccine since 2005, from a Factory in Tuas and are employing over 1,500 trained Singaporeans. They are making HBV vaccines and other vaccines, and other pharmaceutical drugs for the whole world from Singapore.
4. A Cell separator machine (which I had been trained for my Cambridge MD,) was brought in to collect large quantities of HBV plasma, is now used in all hospitals for other purposes: like collecting white cells, platelets and treatment for some acute medical conditions.
5. We introduced legislation to ban imported Aflatoxin, a potent liver carcinogen) which we had found in 4% of ingested cereals in our random population of about 100 subjects (1980) . Also important were the introduction of Drug registration, as we found bad vaccines, entering Singapore without anyone knowing about it ..Many legislation changes arose out of the project. These include requiring checks by special chemical laboratories for chemical toxins and carcinogens in imported food.
6. We upgraded our education system from " a kinder garden" level.... to Industrial Phds., from simple science to industrial level... But... first through IMCB (1985), then to Science Park, to "A" Star... and to so many industries, and universities with our people trained in highest industrial know how... so lacking in the 1975 when I returned home to help here.


A CANCER VACCINE
that transformed Singapore and the world
COMMEMORATIVE BOOK LAUNCH
A CANCER VACCINE

Take Home Message

- Would you come home and help if your country calls you?
- Are you willing to make extraordinary sacrifices in order that lives may be saved?
- Are you willing to give yourself to help others freely and expect nothing back in turn?
- Are you willing to endure humiliation and loneliness in your endeavor not knowing what the end result would be ?
- When going through danger and the unknown do you put your trust in God?

Special Tribute

Tribute to Those Who Helped in the Project

MOH Scientific & Advisory Committee on Hepatitis & Related disorders (1983-)

- Professor Gabriel Oon Chong Jin (Chairman), NUS Department of Medicine I, SGH (1983-97). Stayed till 2005 as member.
- Professor Goh Kee Tai (Secretary), Ministry of the Environment & Quarantine & Epidemiology Department.
- Dr Aw Swee Eng, Head, Nuclear Medicine, SGH
- Professor Chan Soh Har, Director, WHO Immunology Laboratory, NUS
- Dr Ong Yong Wan, Head, National Blood Bank, SGH
- Professor Lee Hin Peng , Singapore Cancer Registry, NUS.
- Dr Jimmy Sng, Department of Pathology, SGH.
- **++Professor Tan Khim Leong**, Head Neonatal Pediatrics, NUS

Tribute to Those Who Helped in the Project

MOH DMS/Permanent Secretary.

- **++Dr Andrew Chew** (1977-1984)
- **++Dr Kwa Soon Bee** (1984-1996)

NUS. Medical Faculty

- **++Professor Edward Tock**, Dean
- **++Professor Wong Poi Kong**, Head, University Department I, SGH

World Health Organisation, Geneva

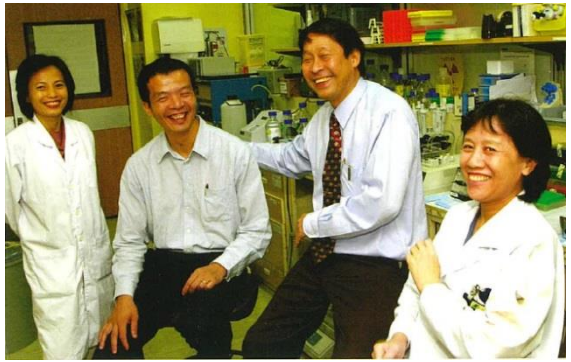
- **++Dr Frank Perkins**, Chief of Biologics
- **++Dr Tomatis**, Director International Agency for Research in Cancer, WHO

++ In Memory of precious colleagues who have passed away,

Tribute to Those Who Helped in the Project

SCIENTISTS & STAFFWHO HELPED IN RANSOME RESEARCH Laboratory:

- Dr Yo Sui Lan Ph. D 1975-83. Started Liver Cancer & HBV research
- Dr Lily Chan Ph. D 1982-85. Industrial QC for Vaccines
- Dr Ren Ee Chee Ph.D. 1982 -85. Industrial Production of HB Vaccine.
- Mrs Lily Wong M.Sc.. 1985. Quality control HBV testings.
- Dr Chen Wei Ning Ph.D. 1997. Innovation, patenting and DNA work.
- Mrs Lim Gek Keow, Senior Laboratory Assistant in charge of Ransome Laboratory.
- **++Sister Rose Smith SRN**. 1984. Research Nurse.
- Sister Leong Kwee Liam, Nursing Officer in KKH.



Thank You