[Singapore]

Current Management of Malignant Diseases

Bertha WOON*1

We present the top cancer in men and women respectively.

Colorectal Cancer

Colorectal cancer

Colorectal cancer is the most common cancer in Singapore, and is the top cancer afflicting men. Its incidence has risen in recent years. Risk factors include age, ethnicity, lack of exercise, obesity, diet, and family history.

Detection

As early colorectal cancer is asymptomatic, regular screening aids early detection. Annual screening using Faecal Occult Blood Test, Double-Contrast Barium Enema, Flexible Sigmoidoscopy, and Colonoscopy for adults aged 50 and above is recommended.

Multidisciplinary management

A multidisciplinary approach is used. Treatment includes surgery (curative resection or bypass operation), radiological intervention (e.g. stents), radiation therapy, chemotherapy (neoadjuvant or adjuvant) regimens such as FOLFOX (FOL—Folinic acid [leucovorin], F—Fluorouracil [5-FU] and OX—Oxaliplatin).

Survival rates

Our overall colorectal cancer survival rate has increased because a majority of the cases are diagnosed at Stage 2. However, the earlier the cancer is diagnosed, the better the survival. Therefore, screening is very important.

Nationwide efforts

The Ministry of Health (MOH) and Health Promotion Board coordinate public education activities, such as Colorectal Cancer Awareness Month. In 2011, MOH announced that those aged 50 and above can use their Medisave funds to pay for a colonoscopy, which can cost around $1,500. Individuals are encouraged to implement lifestyle changes like exercising frequently, maintaining a healthy body weight and eating more fibre. High risk individuals are encouraged to attend screening earlier and more frequently.

Breast Cancer

Breast cancer

Breast cancer is the commonest cancer among women in Singapore. From 1968 to 2002, the local incidence of breast tripled. Of concern to us is the fact that the peak incidence is around 10 years earlier than in the West. Risk factors include age, ethnicity, family history, age at menarche and menopause, parity, age at first live birth, and prior breast biopsies.

Detection

People with genetic risks, including those that have family histories of breast and ovarian cancer, are advised to undergo mammograms. However, mammograms lack sensitivity, and specificity, especially in younger women and in women with dense breasts. By combining mammograms with ultrasound scans, cancer detection can be increased by 10% to 15%.

Management of early breast cancer

Surgery for early breast cancer is minimally invasive and aimed at conservation. Chemotherapy (adjuvant vs neoadjuvant) decisions can be aided by the tumour receptor status as well as tests like Oncotype Dx. Post-operative radiotherapy is essential (standard vs brachytherapy), and hormonal therapy is determined by ER/PR/c-erb-B2 status.

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Management of locally advanced breast cancer (LABC)

Treatment of LABC involves chemotherapy (adjuvant vs neoadjuvant), radiotherapy (standard vs brachytherapy), hormonal therapy, and surgery (skin cover and reconstruction if necessary).

Survival rates

Overall, survival rates of breast cancer cases increased partly due to early detection and better treatment regimens, with a majority of the breast cancer cases are diagnosed at Stage 2 or earlier. The earlier breast cancer is diagnosed, the better the survival. Therefore, screening is paramount.

Current Management of Malignant Diseases

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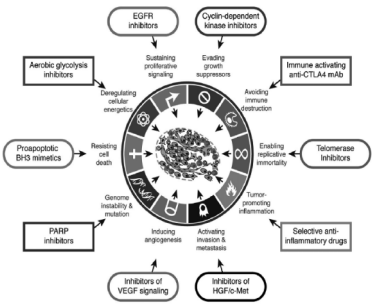
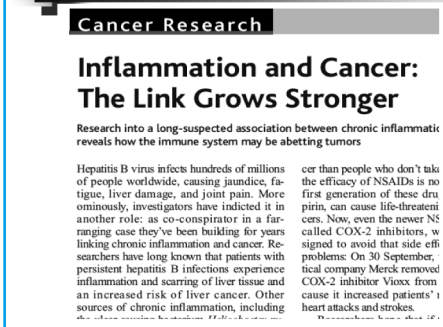
Inflammation as a Hallmark of Cancer



Hallmarks of Cancer – *Cell 2011*

Inflammation as a Hallmark of Cancer



Cancer Research

Inflammation and Cancer: The Link Grows Stronger

Research into a long-suspected association between chronic inflammatic reveals how the immune system may be abetting tumors

Hepatitis B virus infects hundreds of millions of people worldwide, causing jaundice, fatigue, liver damage, and joint pain. More ominously, investigators have indicted it in another role: as co-conspirator in a far-ranging case they've been building for years linking chronic inflammation and cancer. Researchers have long known that patients with persistent hepatitis B infections experience inflammation and scarring of liver tissue and an increased risk of liver cancer. Other sources of chronic inflammation, including

cer than people who don't take the efficacy of NSAIDs is no first generation of these dru pirin, can cause life-threateni cers. Now, even the newer NS called COX-2 inhibitors, w signed to avoid that side effi problems: On 30 September, tical company Merck removed COX-2 inhibitor Vioxx from cause it increased patients' heart attacks and strokes.

Science 2004

Top 10 cancers in Singapore (2005-09)

Rank	In Men	In Women
1	Colo-rectum	Breast
2	Lung	Colo-rectum
3	Prostate	Lung
4	Liver	Corpus Uteri
5	Stomach	Ovary
6	Nasopharynx	Skin (incl. Melanoma)
7	Skin (incl. Melanoma)	Cervix Uteri
8	Lymphoma	Stomach
9	Kidney & Other Urinary	Lymphoma
10	Bladder	Thyroid

Data from Singapore Cancer Registry, 2005-2009, Interim Report

COLORECTAL CANCER

Colorectal cancer

- Colorectal cancer is the number 1 cancer in Singapore
- Number of colorectal cancer cases in Singapore is rising
- 2005-09: 7,909 cases
- 2005-10: 8,206 cases
- An increase of nearly 4%

Some risk factors

- Adults aged > 50 years old
- Race: Chinese have higher risk than Malays or Indians
- Lack of exercise
- Obesity
- Diet: too much red meat, too little fruits and vegetables
- Family history

Detection

- No symptoms in the early stages of colorectal cancer, so regular screening can help to detect the disease early
- Annual screenings for adults aged 50 and above recommended

Detection

- **Faecal Occult Blood Test** – simple test conducted on patient's stool
- **Double-Contrast Barium Enema** – x-ray examination of large intestine
- **Flexible Sigmoidoscopy** – examination of the internal lining of the lower end of large intestine using short, flexible lighted tube
- **Colonoscopy** – examination of the entire large intestine using longer, flexible lighted tube

Multidisciplinary Treatment

- **Surgery**
  - To remove the cancerous growths
    - Tendency for minimally invasive surgery
    - Functional restoration
    - Multi-disciplinary
  - To bypass obstruction
    - Staged operations
    - Permanent diversion
- **Radiological intervention** e.g. stents

Treatment

- **Chemotherapy** to destroy cancer cells after surgery, to control tumour growth or to relieve symptoms of colorectal cancer
  - Adjuvant
  - Neoadjuvant
- FOLFOX
  - FOL – Folinic acid (leucovorin)
  - F – Fluorouracil (5-FU)
  - OX – Oxaliplatin (Eloxatin)

Chemotherapy - What Have We Learnt?

- **All the "progress" that has been made so far with the only exception of FOLFOX was really one of "less pain but same gain"**
  - **Shorter duration of treatment**
  - **More convenient administration**
  - **Less side effects**
  - **But similar efficacy**

FOLFOX was the only real step forward since 5FU/LEV in 1990

Negative Irinotecan studies

Negative Bevacizumab studies

Negative Cetuximab studies

Treatment

- **Radiation therapy**
  - Adjuvant
  - Neoadjuvant to shrink large tumours before an operation so that they can be removed more easily
  - Relieve symptoms of colorectal cancer

Survival rates

- An overall increase in survival rate of colorectal cancer cases
- Majority of the colorectal cancer cases are diagnosed at Stage 2 or later
- However, the earlier that colorectal cancer is diagnosed, the better the survival
- Therefore, screening is paramount

Nationwide efforts

- Public education activities coordinated by the Ministry of Health and Health Promotion Board, e.g., Colorectal Cancer Awareness Month
- In 2011, the Ministry of Health announced that those aged 50 and above can now use their Medisave funds to pay for a colonoscopy, which can cost around $1,500

Nationwide efforts

- Individuals belonging to the high risk group should have screenings earlier and/or more frequently
- Individuals should also implement lifestyle changes like exercising frequently, maintaining a healthy body weight, eating more fibre, etc.

BREAST CANCER

Introduction

- Breast Cancer is the commonest cancer among women in Singapore
- From 1968 to 2002, the incidence of breast cancer increased three-fold
- The average age of onset is about 10 years earlier than in the West
- Peak incidence is 50-59 years but there is another earlier peak in the late 30s to early 40s

More facts and figures…

- Breast cancer occurs in around 1 in 8 cancers in Singaporean women.
- Every year, about 1,000 new cases of breast cancer are diagnosed. This translates to about 3 women being diagnosed with breast cancer each day.
- About 260 die from the disease each year.
- 1 in 20 women in Singapore will be diagnosed with breast cancer in their lifetime.

Risk Factors

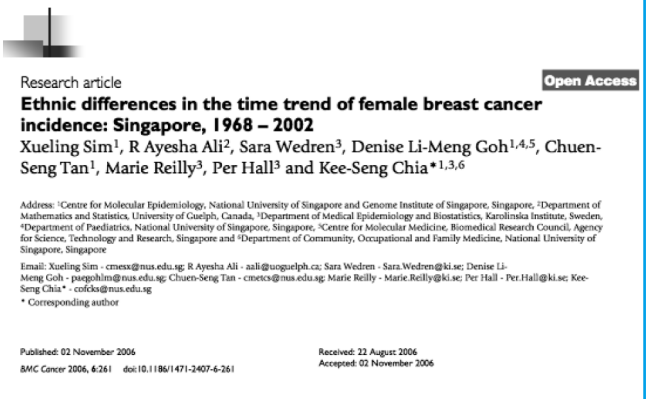
- **Age, Ethnicity/race**
- **Family history**
- **Age at menarche; age at menopause**
- **Parity**
- **Age at first live birth**
- **Prior breast biopsies: Atypical ductal hyperplasia, sclerosing adenosis or LCIS**
- **Prior thoracic irradiation (e.g., Hodgkin's disease)**
- **Known or suspected BRCA1, BRCA2, p53, PTEN, or other gene mutation associated with breast cancer risk**
- **Current or prior estrogen and progesterone hormone replacement therapy**

BREAST CANCER -- 2012

TABLE 1. BREAST CANCER SINGAPORE FEMALES, 2005-2009 – TOP FEMALE CANCER & TOP CANCER DEATHS [17.8% ALL FEMALE CANCER DEATHS]

Ethnic group	Number (%)	CR (95% CI)*	ASR (95%c CI)**
All	7,458 (29.4)	82.3 (80.4 – 84.2)	60.0 (58.6 – 61.3)
Chinese	6,029 (28.3)	88.3 (86.1 – 90.5)	60.8 (59.1 – 62.3)
Malay	842 (34.3)	68.6 (63.9 – 73.2)	58.7 (54.6 – 62.8)
Indian	438 (37.9)	57.5 (52.1 – 62.9)	53.8 (48.6 – 59.0)

* CR = Crude rate per 100,000 per year
** ASR = Age standardised rate per 100,000 per year. ASR derived by direct method using the "World Population"
SOURCE: Singapore Cancer Registry, NDRO



Research article

Open Access

Ethnic differences in the time trend of female breast cancer incidence: Singapore, 1968 – 2002

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Abstract

Background: From 1968 to 2002, Singapore experienced an almost three-fold increase in breast cancer incidence. This increase appeared to be different across the three main ethnic groups: Chinese, Malays and Indians. This paper used age-period-cohort (APC) modelling, to determine the effects of age at diagnosis, calendar period, and birth cohort on breast cancer incidence for each ethnic group.

Methods: This study included all breast cancer cases (n = 15,269) in the three ethnic groups, reported to the Singapore Cancer Registry from 1968 to 2002 between the ages 25 to 79. Age-specific fertility rates from the Department of Statistics were used to explore the role of fertility.

Results: In the 1970s, Indian women had the highest age-standardized breast cancer but by the mid-1980s the highest rates were seen among the Chinese. Remarkable differences were seen in the age-specific incidence rates by ethnic groups. After age 49, the incidence rates for the Chinese and Malays leveled off whereas it continued to rise in the Indians. While our analyses provided some evidence that an age-drift model described the trend seen in the Indians, age-period-cohort model and age-cohort model had the best fit for the Chinese and Malays aged 25 to 79 respectively. Overall, Chinese and Malay women born in later cohorts were at increased risk of developing breast cancer relative to their counterparts in the earlier cohorts. The three ethnic groups experienced similar changes in their fertility in the 1970s, which likely explained much of the increase in their breast cancer incidence but not the ethnic differences. There was a stronger inverse association between total fertility rate and pre-menopausal breast cancer incidence in the Chinese and Malays than the Indians.

Conclusion: The observed dissimilarity among ethnic groups suggests ethnic differences in exposure or response to certain risk factors. It is likely that longer and subtler differences in childbearing trends and other risk factors may further explain these ethnic differences.

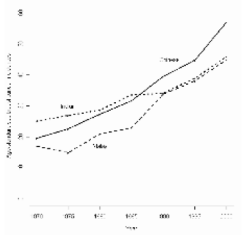


Figure 1
Age-standardized incidence rates of breast cancer stratified by ethnic group from 1968 to 2002 (as indicated by the mid-year of the 5-yearly intervals).

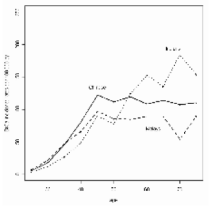


Figure 2
Overall age-specific breast cancer rates stratified by ethnicity and 5-yearly diagnosis period from 1968 – 2002 (as indicated by the first year of the 5-yearly intervals).

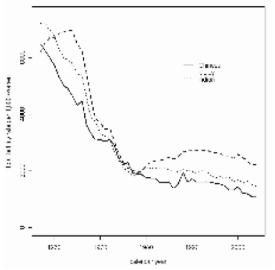


Figure 4
Total fertility rates for Singaporean women aged 15 – 44 from 1968 – 2002, stratified by ethnicity. Source: Reports on Registration of Births and Deaths (1968 – 2002). (Note: Only number of live births in each year is included and female population denominators used are based on interpolation of census data in 1970, 1980, 1990 and 2000).

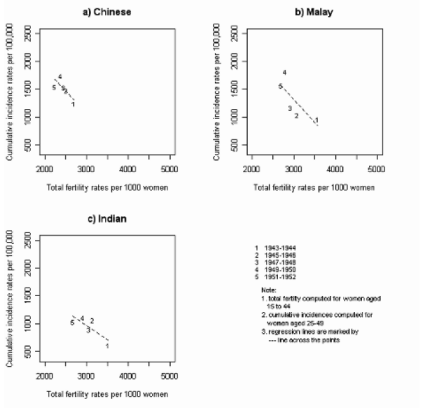


Figure 5
Scatterplots of cumulative breast cancer incidence rates per 100,000 women (for ages 25 to 49) and total fertility per 1,000 women (for ages 15 to 44) for cohorts 1943 – 1944, 1945 – 1946, 1947 – 1948, 1949–1950 and 1951–1952. Over time, decreased total fertility seems to be associated with increased cumulative rate of breast cancer incidence across three ethnic groups.

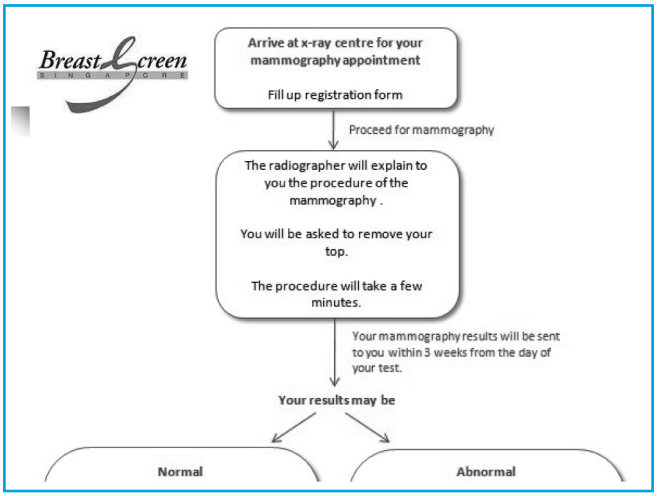
Management

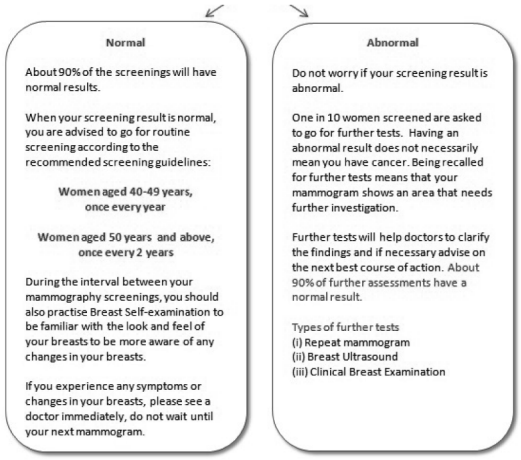
- Multidisciplinary team approach
- Primary care physician
- Surgeon
- Medical oncologist
- Radiation oncologist
- Radiologist
- Pathologist

Primary Physician and Surgeons to screen People with genetic risks

- Breast cancer diagnosed ≤ 40 years
- Personal history of breast cancer and ovarian cancer
- Personal history of breast cancer and close male blood relative with breast cancer
- Personal history of breast cancer diagnosed ≤ 50 years or 2 breast primaries, and ≥ 1 close blood relative with breast cancer ≤ 50 years and/or ≥ 1 close blood relative with epithelial ovarian cancer

MOH CPG – Cancer screening, 2010





Limitations of mammogram

- Mammogram is far from an ideal screening test. It lacks sensitivity, and specificity of an ideal screening test and is particularly problematic in younger women and in people with dense breasts
- Combination with ultrasound breasts can increase cancer detection by 10-15%

Issues faced by Surgeons as Intermediary doctor

- Coordinator – primary point of contact
- How to strike a balance between
  - Radiologist's and pathologist's reports
  - Delayed diagnosis vs overdiagnosis and treatment
  - Excessive investigations vs missing a cancer
  - Limitations of technology and patient expectations

Management early breast cancer

- Surgery
  - Minimally invasive / conservation
  - Immediate vs delayed reconstruction
- Chemotherapy
  - Adjuvant vs neoadjuvant
  - Oncotype Dx
- Radiotherapy
  - Standard vs brachytherapy
- Hormonal therapy
  - Determined by ER/ PR/ c-erb-B2 status

Management locally advanced breast cancer

- Chemotherapy
  - Adjuvant vs neoadjuvant
  - Oncotype Dx
- Radiotherapy
  - Standard vs brachytherapy
- Hormonal therapy
- Surgery
  - Skin cover and reconstruction if necessary at all

Survival rates

- Overall survival rate of breast cancer cases is increased partly due to early detection and better treatment regimens
- Majority of the breast cancer cases are diagnosed at Stage 2 or earlier
- The earlier breast cancer is diagnosed, the better the survival
- Therefore, screening is paramount

THANK YOU