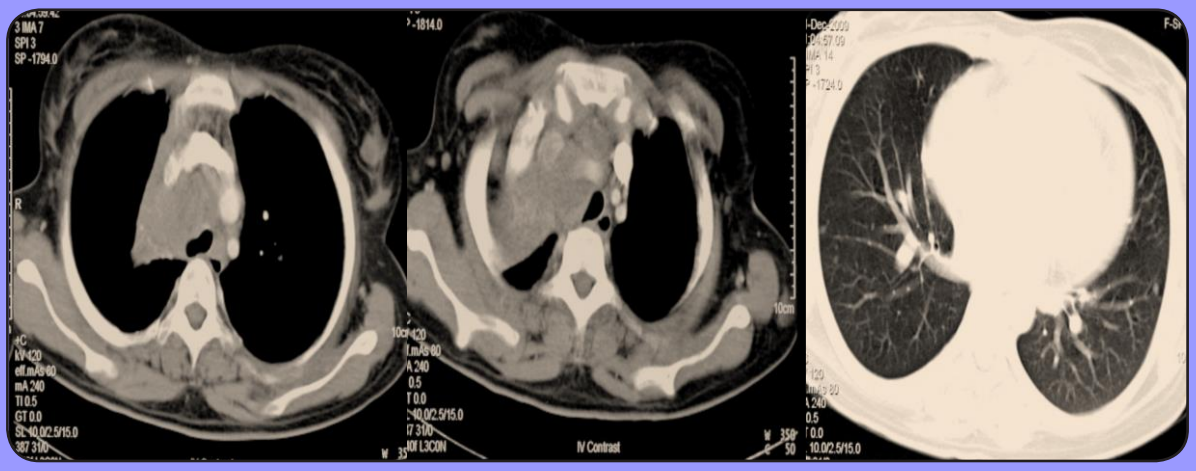
JUMMEC



Vol. 15 Issue 1 2012

Journal of Health and Translational Medicine

UNIVERSITI MALAYA

Vol. 15 Issue 1 2012

JUMMEC

Journal of Health and Translational Medicine

UNIVERSITI MALAYA

JUMMEC

Journal of Health and Translational Medicine

Volume 15 Number 1 **2012**

UNIVERSITI MALAYA

JUMMEC

Volume 15 Number 1 **2012**

Correspondence

All manuscripts, general correspondence and enquiries should be addressed to: Journal of Health and Translational Medicine (JUMMEC), The Dean's Office, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, MALAYSIA.

Publisher

The Journal of Health and Translational Medicine (*JUMMEC)* is published two times a year by the University of Malaya Medical Centre. An online archive of *JUMMEC* issues is available through the website: jummec.um.edu.my.

Aim and Scope

JUMMEC publishes both basic and applied science as well as clinical research studies on any area of medicine that is of interest and relevance to the medical community. This is a peer-reviewed Journal that publishes twice yearly on Review Articles, Original Articles, Short Communications, Clinico-pathological conference abstracts, Case Reports, Letters to the Editor and Book Reviews.

Manuscript Submission

We welcome journal submissions throughout the year but preferably by **March** and **September**. Articles submitted for publication are understood to be offered only to *JUMMEC* and which have not been sent to other journals for consideration.

Cover

Computed tomography thorax showed right upper lobe mass with associated upper lobe collapse, multiple mediastinal lympadenopathy and left breast mass and multiple lung nodules. Image courtesy of Ng Teck Han

Instructions for Authors

The **Journal of Health and Translational Medicine (JUMMEC)** publishes both basic and applied science as well as clinical research studies on any area of medicine that is of interest and relevance to the medical community. This is a peer-reviewed journal that publishes Reviews Articles, Original Articles, Short Communications, Clinico-pathological Conference Abstracts, Case Reports, Letters to the Editor and Book Reviews.

Articles submitted for publication are understood to be offered only to JUMMEC and which have not been sent to other journals for consideration.

The Manuscripts

Send manuscripts to: http: //jummec.um.edu.my

or write in to: Editor-in-Chief Journal of University Malaya Medical Centre (JUMMEC) The Dean's Office Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, MALAYSIA. Fax: (603) 7956 8841 Email: jummec@um.edu.my

Manuscripts submitted to JUMMEC should be prepared according to the American Medical Association (AMA) Manual of Style (10th edition). We accept articles written in either British English or American English but the language usage should be consistent throughout the manuscript.

Each manuscript component must begin on a new page in the following sequence: (1) title page; (2) abstract and keywords;

(3) text; (4) acknowledgements; (5) references; (6) figure legends;

(7) tables; and (8) figures. Please submit figures as separate figure files (jpeg or gif) with 300 dpi resolution or better.

Type manuscript double-spaced throughout. Number pages consecutively commencing on the title page.

Articles should be not more than 3,000 words.

The Title Page

The title page should contain a concise title of the article. Names of authors who have contributed to the writing of the manuscript should be written in style of initials followed by surname or preferred name, eg. Saleena VEO, Anita S or Brown J. Add at the bottom of the phrase "Address for correspondence;" followed by full name and address with postal code and email address.

The Abstract

Limit the number of words to 150. It should state the purpose of the study, a brief description of the procedures employed, main findings and principal of conclusions. At the end of the abstract, please include an alphabetical list of 3-5 keywords and subjects for indexing. Choose the appropriate keywords as these will be used for subsequent retrieval.

The Text

It should consist of an Introduction, Methods, Results, Discussion and Conclusion/Recommendation. Systeme Internationale (SI) Units should be used. Use only standard abbreviations. The full term for which an abbreviation stands should precede its first use in the text unless it is a standard unit of measurement.

References

Number the references in the order of mention in text. References in the text should be indicated by a figure within parenthesis e.g. (1, 2,). Limit references to 30, if possible. Identify references in text, tables and legends.

The titles of journals in the list should be abbreviated according to the Index Medicus.

Authors are responsible for the accuracy of all references. The editor can only check for correctness of format. Follow the examples of forms of references as shown below.

Journal references should be cited as follows:

Stewart AL, Mills KM, King AC, *et al*. CHAMPS Activities questionnaire for older adults. *Med Sci Sports Exerc* 2001; 33(7): 1126-1141.

Kaneda T. Health care challenges for developing countries with aging populations. Populations Reference Bureau. Available from http://www.prb.org/Articles/2006/HealthCare ChallengeswithAgingPopulations.aspx. Accessed 21 Mar 2007.

Book chapters should conform to the following:

Skinner MW, Holden LK, Binzer SM. Aural rehabilitation for individuals with severe and profound impairment hearing aids, cochlear implants, counseling and training. In: Valente M. ed. *Strategies for Selecting and Verifying Hearing Aid Fittings*. NY: Thieme Medical Publishers; 1994: 267-299.

Books should be listed as:

Baselt RC, Cravey RH. *Disposition of Toxic Drugs and Chemicals in Man.* 8th ed. Foster City, Calif: Chemical Toxicology Institute; 2008.

Iverson C, Flanagin A, Fontanarosa PB, Glass RM, Glitman P, Lantz JC, *et al*. American Medical Association manual of style: a guide for authors and editors. 9th Ed. Baltimore: Williams & Wilkins; 1998.

Tables

Start each table double-spaced on a separate sheet. Do not submit tables as photographs. Give each table a number in order of mention in text. Provide footnotes for explanatory matter and identify in alphabetical order all abbreviations used. Place all tables and figures at the end of the manuscript after the references. You may place callouts for the table and figures in the text. For example, write "INSERT TABLE 1 HERE" to show where the table should appear within the text. All tables should be prepared for publication vertically.

Illustrations

Authors are advised to submit figures as JPEG, TIFF or GIF formats; PowerPoint slides and images embedded in Word documents *do not* transfer well to print unless they are simple line art. Abbreviations, arrows, symbols, numbers or letters used in the figures are to be identified and explained in the corresponding legends.

Submit written permission from the copyright holder to reproduce any previously published figures. Colour photographs will be published at the author's expense.

Disclaimer

Neither the editors nor the publishers accept responsibility for the views of authors expressed in the contributions.

Forewords from the Editor

Dear Readers of JUMMEC,

Welcome to the first issue of the Journal of Health and Translational Research's (JUMMEC) in the year 2012. The current issue consists of one review on improving cancer survivorship, one short communication on leishmaniasis in Southeast Asia, one case report on a rare metastasis to the breast, and a guest editorial on a physiologic journey.

The case report highlights a rare case of metastatic disease to the breast from a primary lung adenocarcinoma in a young 22-year-old lady. The importance of distinguishing a primary breast cancer from a metastasis to the breast is reiterated as the therapeutic planning and the outcome between them are different. The review article on improving cancer survivorship presents a brief overview on the importance of adopting healthy behaviour during and after the completion of primary cancer treatment. Both realms of activity and inactivity are now acknowledged as influential independent factors contributing to better care in the field of cancer survivorship. The short communication on leishmaniasis in Southeast Asia aims to make the readers aware of the existence of this new emerging infective disease. Although this disease is uncommon outside Middle Eastern countries, it should be considered as a probable diagnosis even in non-endemic countries since its early identification can lead to better cure rates and prevent early fatality.

The highlight of this issue is a guest editorial article written by Professor Hwee Ming Cheng, which describes his 'Physiologic Journey' in the land of Academia during his inaugural lecture in 2011. In this article, Professor Cheng has highlighted some of his discoveries in the field of immunology, as he followed the wise words of an immunologist, JR Marrack, "The secret of successful research is to ask nature, simple questions, one at a time". Many of Professor Cheng's discoveries were described as serendipitous but as Louis Pasteur said, "In the field of observation, chance favours only the mind which is prepared." Thus, these serendipitous or chance discoveries serve only to reveal how prepared a mind Professor Cheng has in the area of laboratory observation. Professor Cheng not only excels in research he is also an inspiring teacher and a wise friend to many of his students. He has written many books on the teaching of Physiology and initiated the Inter-Medical School Physiology Quiz (IMSPQ), which has now become international – all these you can read in his article. As a fellow colleague, a research collaborator, a longtime family friend and an ex-classmate of Professor Cheng, it gives me great pleasure to feature Professor Cheng's inaugural lecture as the spotlight article in this issue.

We hope you will find the articles in this issue both interesting and relevant in your respective fields of research as well as providing a useful reference to your future research undertakings.

With best wishes,

Debra Si Mui Sim
Editor,
The Journal of Health and Translational Medicine.

FROM THE LUNG TO THE BREAST: A YOUNG LADY IN DISTRESS – A CASE REPORT AND LITERATURE REVIEW

Ng TH[1], How SH[1], Kuan YC[1], Salmah B[2]

1 Department of Internal Medicine, International Islamic University Malaysia, Kuantan, Pahang
2 Department of Pathology, Faculty of Medicine, MARA Technology University, Shah Alam, Selangor

Correspondence:

Associate Professor Dr. Ng Teck Han
Kulliyyah of Medicine,
International Islamic University Malaysia,
27510 Kuantan
Pahang, Malaysia.
E-mail: ngteckhan@hotmail.com
Tel: 609-5133 710 Ext 3331
Fax 609-5177 631

ABSTRACT

Metastases to the breast from non-mammary malignant neoplasm are relatively rare. We report a case of metastatic disease to the breast from a primary lung adenocarcinoma in a young 22-year-old lady. Computed tomography of the thorax confirmed right upper lobe mass with multiple lung nodules and a breast lump. The diagnosis of breast metastasis was confirmed by fine needle aspiration cytology of the breast lump with histopathological findings and immunohistochemical features consistent with lung adenocarcinoma. *(JUMMEC 2011; 14(2))*

KEYWORDS: *lung cancer, breast metastasis, immunohistochemical staining*

Introduction

Breast cancer is the most common malignancy in women accounting for about 30% of all female malignancies and the leading cause of death for women ages 35-54 years (1). Breast metastasis from lung primary is unusual. There was only a handful of cases reporting breast metastasis from lung cancer in the past (1-7). We report a case of metastatic disease to the breast from a primary lung adenocarcinoma in a young 22-year-old lady.

Case report

A 22-year-old previously healthy married woman, who was a passive smoker, presented to us with 3 days of fever, productive cough with greenish sputum and mild haemoptysis. In the preceding 4 months, she had intermittent dry cough, lethargy with significant loss of appetite and weight. She also had hoarseness of voice for one month and painless left forearm swelling 2 months prior to presentation. The patient was thin, pale and had no clubbing or jaundice. There were multiple hard cervical, submandibular, supraclavicular and posterior auricular lymphadenopathy (the sizes ranged from 0.5 to 2 cm). There was no axillary or inguinal lymphadenopathy. There was a non-tender 2 x 2 cm bony swelling over the upper one third of the left humerus. The liver was enlarged, 3 cm below the subcostal margin. There was a discrete, 2 x 2 cm, non-tender, well circumscribed, firm, and mobile breast lump located at the left upper outer quadrant of the left breast without any associated skin or nipple changes. Clinically, it felt benign. The patient herself was not aware of the breast lump at all. There were no significant findings on lung examination and other systemic examination. Flexible laryngoscopy revealed right vocal cord paralysis.

Investigations revealed hypochromic and normocytic anaemia (haemoglobin 8.5 g/dL) with thrombocytosis (platelet 555 x 10^9/L) and mild leukocytosis (total white cell count 11.22 x 10^9/L). Serum electrolytes, calcium, phosphate and liver function tests were normal. A chest roentgenogram showed right upper lobe segmental collapse. Left humerus X-ray showed a lytic lesion and periosteal reaction of the upper one third of the humerus. Computed tomography (CT) of the thorax confirmed right upper lobe mass with right apical segmental collapse and mediastinal lymphadenopathy. Multiple lung nodules in both lung fields and a left breast lump were also seen (Figure 1). CT of the abdomen and pelvic region were normal. MRI of the humerus revealed a focal lesion in the upper left humerus with extra-medullary extension

suggestive of malignancy. Fine Needle Aspiration Cytologycal (FNAC) examination of the breast lump and cervical lymph node confirmed adenocarcinoma of lung cancer as a primary tumour which was supported by the immunohistochemical staining. Thyroid transcription factor-1 (TTF-1) and cytokeratin (CK) 7 were consistently positive in the left breast lump, left post-auricular swelling and right submandibular lymph node, while stains for CK20, Estrogen receptor, Progesterone receptor and thyroglobulin were negative (Figure 2). The patient defaulted follow up and opted for traditional treatment. She succumbed to advanced lung cancer 4 months after diagnosis.

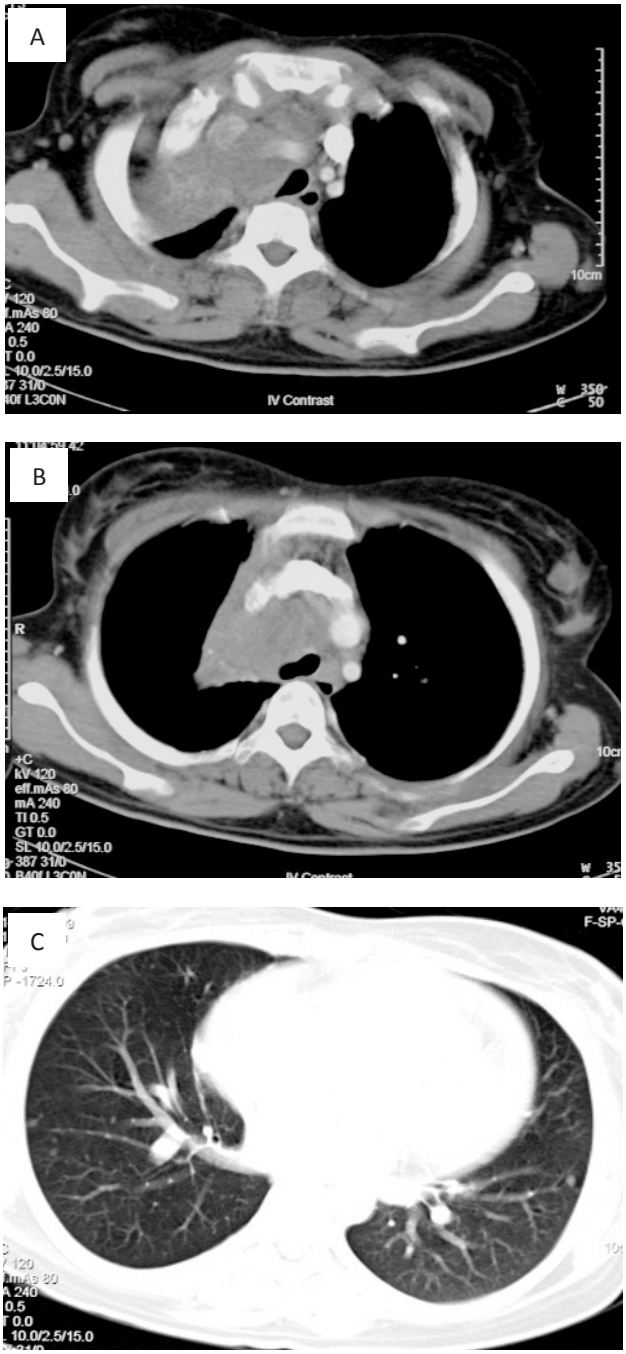


Figure 1: *Computed tomography thorax showed right upper lobe mass with associated upper lobe collapse (A), multiple mediastinal lympadenopathy and left breast mass (B) and multiple lung nodules (C).*

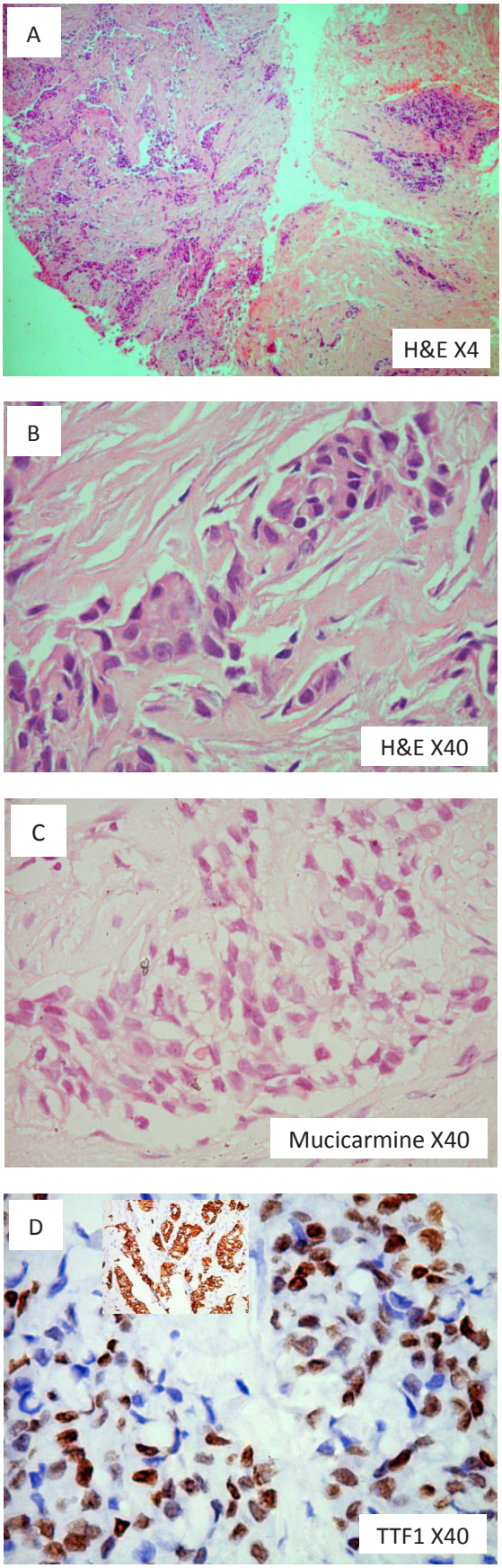


Figure 2: *Biopsy of the left breast lump showed islands of infiltrating malignant cells(A) with poorly formed glandular structures (B). Scattered cells showed intracytoplasmic mucin, arrow(C). The tumour cells were positive for CK7 (insert) and TTF-1(D)*

Discussion

Breast metastases from non-mammary tumours are rare, which account for 0.5% to 1.3% of all breast cancers (2). Tumours most commonly metastasising to the breast are malignant melanoma, lymphoma, and leukaemia (3). The usual sites of distant metastasis for lung cancer are liver, bone, brain, lung and adrenal gland (3). Breast metastasis from lung primary is unusual. The characteristic of some cases are summarised in Table 1. It is noteworthy that the patient in our case report is only 22 years old, which makes her the youngest patient ever reported to have breast metastasis from lung cancer. Based on the published case reports on lung cancer metastasised to the breast, the ages of the patients ranged from 39 to 81 years old (1-7). Clinically, it can be difficult to differentiate a benign from a malignant breast lump. A number of "classic" characteristics of breast cancerous lesions have been described such as single lesion, hard, immovable, irregular borders and size ≥2 cm. However, these features individually do not distinguish well between cancers and benign lesions because a significant number of malignant lesions were soft or cystic (38 percent), freely movable (61 percent), regular (41 percent), and less than 2 cm in size (28 percent) in the study conducted by Venet *et al* (8). Direct involvement of the underlying chest wall or skin with oedema (including peau d'orange) or ulceration or satellite skin nodules confined to the same breast or dimpling or nipple retraction connote locally advanced breast tumour (9). The physical examination had a positive predictive value of 73 percent and a negative predictive value of 87 percent for breast cancer (10).

The majority of the case reports published previously revealed that the breast lump appears benign clinically. The metastatic breast lump was usually described as single or multiple discrete masses, non-tender in nature with the size ranging from 0.8 cm to as large as 6 cm in diameter. The majority of the metastatic lumps were situated in the outer quadrant of the breast, which likely represented haematogenous spread (2, 3, 4, 7). All cases of breast metastasis were confirmed by histo-pathological examination (HPE) of the excision biopsy or fine needle aspiration cytology (FNAC) and/or immunohistochemical profile. It may be difficult also to differentiate a primary breast cancer from a metastatic disease. An incorrect diagnosis can lead to unnecessary surgical intervention. Therefore, any suspicious lump should be biopsied to confirm the nature of the mass. HPE with immunohistochemical test is a key point for diagnosis as all cases were confirmed in this manner. Immunohistochemical test is very helpful to differentiate the site of the primary tumour. In our patient, the diagnosis was made through immunohistochemical test and FNAC. Ideally, tissue from both lung nodules should be sampled for morphology and immunohistochemical profile comparison, but the patient was lost to follow up. To our knowledge, there is no reported TTF-1 positivity in primary breast carcinoma (11-14). Thorough morphologic assessment together with support from panels of immunohistochemical stains and special stains are able to indicate the most likely primary source of malignancy.

In conclusion, breast metastasis should always be considered in a patient with lung cancer presenting with a breast lump. The ultimate diagnosis of breast metastasis should involve histopathological confirmation of biopsy or FNAC specimens with the help of immunohistochemical test. It is important to distinguish a primary breast cancer from a metastasis to the breast, as the therapeutic planning and the outcome between them are different.

Table 1: *Summary of the reported cases of breast metastasis from lung cancer*

Author	Cell type	AGE	Gender	Clinical feature of the breast lump				Diagnosis by	Prognosis (survival since diagnosis)	Treatment
				Location	Feature	Skin changes	Axilarry LN			
Rimner A et al (1)	Large cell	49	Female	Superior outer quadrant of left breast	Mass 6 x 5 x 4 cm, with mastitis, no axillary LN	nil	nil	Biopsy (HPE)	7 months	Palliative radiotherapy
Rimner A et al (1)	Adenocarcinoma	81	Female	Medial and lateral left breast	Multiple masses, painless, hard. up to 4 x 1.2 x 1.9 cm	nil	Palpable	FNAC (HPE and immunohistochemistry)	-	Palliative radiotherapy
Sadikot RT et al (2)	NSCLC	47	Female	Left upper outer quadrant	2 discrete, non tender, mobile lumps	nil	nil	FNAC	-	-
Gomez-Caro et al (3)	Adenocarcinoma	65	Male	Left breast	Single mass	nil	nil	FNAC (HPE and immunohistochemistry)	-	Radical mastectomy followed by chemotherapy
Luh SP (7)	SCLC	66	Female	Left upper and lower quadrant	2 discrete masses (3 and 0.8cm), firm	nil	palpable	Excision biopsy (HPE and immunohistochemistry)	-	Left mastectomy

References

1. Georgiannos SN, Aleong JC, Goode AW, Sheaff M. Secondary neoplasms of the breast. A survey of the 20th century. *Cancer* 2001; 92: 2259-66.
2. Rimner A, Rosenzweig KE. Palliative radiation for lung cancer metastases to the breast: Two case reports. *J Thorac Oncol* 2007; 2: 1133-35.
3. Sadikot RT, Renwick DS, Dacosta P, Chalmers AG, Pearson SB. Breast metastasis from non-small cell lung cancer. *Southern Med J* 1997; 90: 1063-64.
4. Gomez-Caro A, Pinero A, Roca MJ, Ferri B, Galindo PJ, Parrilla P. Surgical treatment of solitary metastasis in the male breast from non-small cell lung cancer. *Breast J* 2006; 12: 366-67.
5. Masmoudi A, Mathieu MC, Soria JC. Breast metastasis from lung adenocarcinoma: a case report. *Anticancer Res* 2003; 23: 1825-6.
6. Babu KS, Robert F, Bryden F, McCafferty A, Downer P, Hansell DT *et al*. Metastases to breast from primary lung cancer. *J Thorac Oncol* 2009; 4: 540-2.
7. Luh SP, Kuo C, Tsao TC. Brest metastasis from small cell lung cancer. *J Zhejiang Univ Sci B* 2008; 9: 39-43.
8. Venet L, Strax P, Venet W, Shapiro S. Adequacies and inadequacies of breast examinations by physicians in mass screening. *Cancer* 1971; 28: 1546.
9. Gueth U, Wight E, Schoetzau A, Langer I, Dieterich H, Rochlitz C *et al*. Non-inflammatory skin involvement in breast cancer, histologically proven but without the clinical and histological T4 category features. *J Surg Oncol* 2007; 95: 291-7.
10. van Dam PA, Van Goethem ML, Kersschot E, Vervliet J, Van den Veyver IB, De Schepper A *et al*. Palpable solid breast masses: Retrospective single and multimodality evaluations of 201 lesions. *Radiology* 1988; 166: 435-9
11. Matosa A, Singh K, Jacob R, Greaves WO, Tavares R, Noble L *et al*. Comparison of thyroid transcription factor-1 expression by 2 monoclonal antibodies in pulmonary and nonpulmonary primary tumors. *Appl Immunohistochem Mol Morphol* 2010; 18: 142-9.
12. Moldvay J, Jackel M, Bogos K, Soltesz I, Agocs L, Kovacs G *et al*. The Role of TTF-1 in differentiating primary and metastatic lung adenocarcinomas. *Pathology Oncology Research* 2004; 10: 85-8.
13. Stenhouse G, Fyte N, King G, Kerr KM. Thyroid transcription factor-1 in pulmonary adenocarcinoma. *J Clin Pathology* 2004; 57: 383–87.
14. Zhu W, Michael CW. WT1, Monoclonal CEA, TTF-1, and CEA antibodies in the differential diagnosis of lung, breast, and ovarian adenocarcinomas in serous effusions. *Diagnostic Cytopathology* 2007; 35: 370-75.

IMPROVING CANCER SURVIVORSHIPS: TARGETING PHYSICAL ACTIVITY AND INACTIVITY AT TEACHABLE MOMENTS

Loh SY, Chew SL

Dept of Rehabilitation, Faculty of Medicine, University of Malaya, Kuala Lumpur

Correspondence:

Loh Siew Yim
Dept of Rehabilitation, Faculty of Medicine,
University of Malaya, 50603 Kuala Lumpur.
Email: syloh@um.edu.my

ABSTRACT

This article presents a brief overview on the importance of adopting healthy behavior during and after the completion of primary cancer treatment. Increasing evidences are advocating physical activity engagement in cancer survivors due to its convincing beneficial outcomes. Today, outcomes from numerous trials confirmed the need to examine beyond physical activity engagement, into physical inactivity as an independent factor for cancer recurrences. Reducing cancer-risk related behaviors via increase physical activity and reduce inactivity is now receiving much attention in the field of cancer survivorship. Both realms of activity and inactivity are now acknowledged as influential independent factors contributing to better care in the field of cancer survivorship.

Keywords: *cancer survivorship, physical activity, lifestyle redesign, occupational therapy*

Introduction

The National Cancer Institute Office of Cancer Survivorship in America defines a cancer 'survivor' as anyone diagnosed with cancer, from the time of diagnosis to the end of life (1). Two factors have contributed to the steep rise of cancer survivors:

i) advanced cancer treatment and
ii) an aging population (2,3).

Cancer treatments are often invasive and prolonged with unique psychological, physical, social and existential impact upon survivors (4). As breast cancer now takes a form of chronic disease (5), greater efforts are needed to ensure sustainable and relevant health-promoting programs for cancer control. Fortunately, genetic defects play its role in only five to 10 percents of all cancer cases, whereas the remaining 90 to 95 percents are rooted in the environment and lifestyle factor matrices (6). It is also important to state that not all sequela from cancer are negative as survivors will attest that a cancer diagnosis also brings out the positive feelings in them. The sequela of cancer ranges from one end of the continuum to the other end, i.e. from positive feelings of surviving (I am thankful to be alive, each day is a bonus, etc) to negative consequences (constantly living in fear recurrence, facing long term side effects, etc) as expressed by cancer survivors. In the words of a cancer patient before he succumbed to pancreatic cancer at the age of 49 yrs old -

'If God would give him another chance, he will lead a less sedentary and a healthier life'.

This expression reflects the opportunity which cancer researchers have termed as, the 'teachable moment' i.e. when survivors can be challenged and are more willing to accept ideas of positive healthy behavioral changes (7). However, more research is needed to uncover with clarity if a "teachable moment" occurs shortly after the cancer diagnosis, during cancer treatment, or sometime after treatment has been completed, or if it varies from individual to individual.

With more cancer patients surviving more than 5 years beyond diagnosis, the focus from acute care to managing the long-term health consequences of cancer must be shifted accordingly. Having a longer, indefinite period to live, cancer survivors are faced with the vast array of after-effect of treatment. Table 1 highlights some effects that may possibly be ameliorated with physical activity intervention, and where greater support to move on to live healthily can only bring positive impact into their remaining lives. However, for decades, host factors such as weight and physical activity in the overall treatment of breast cancer patients have been disregarded until recently (8), despite the identification of World Health Organization (WHO) that physical activity (PA) is among the nine modifiable risk factor for cancer (9). The aim of this paper is to present a brief overview of the role of physical activity and inactivity as a potential influential factor in improving the quantity and quality of life of cancer survivors. The review also highlights the health behavior recommendations for cancer survivors outlined by an American Cancer Society expert panel.

Table 1: Common side effects of cancer treatment (10)

Surgery	• 'Pulling' sensation over the scar • Scar contracture • Paraesthesia in the axilla and medial upper arm from the necessary dissection of the intercostal brachial nerve at the time of an axillary clearance • Lymphoedema • Physical imbalance and difficulties with muscular neck pain due to breast tissue loss (usually only a problem for women with larger breasts) • Intermittent fleeting, jabbing neurological pains in the breast • Intermittent pain in the upper arm on the side of an axillary clearance (typically settles over 3–6 months)	
Radiotherapy	• Breast oedema and tenderness • Hyperpigmentation in the first year • Might evolve to increased density of the breast tissue • In-field telangiectasia (particularly in the inframammary region and the tumor bed RT 'boost' area) • Small decrease in the size of the residual breast tissue may occur	
Chemotherapy	• Tiredness/fatigue • Hair loss • Bitter taste in mouth is unlikely to linger for more than a few weeks after chemotherapy • Peripheral neuropathy may persist	
Hormonal therapy	➢ Tamoxifen • Hot flushes • Tender breasts • Gastrointestinal upset • Vaginal dryness and discharge • Decreased libido • Abnormal vaginal bleeding endometrial carcinoma and DVTs are rare	➢ Aromatase inhibitors (AI) • Hot flushes • Musculoskeletal pain (can be severe, requiring AI treatment to cease) • Vaginal dryness • Osteoporosis

Physical activity during cancer survivorship

We searched MEDLINE, EMBASE, CINAHL, Web of Knowledge, there were a total of 25 systematic reviews and meta-analysis conducted from the year of 2006 to 2011, using the key searching word, 'physical activity', 'cancer', 'systematic review', 'meta-analysis'. Cancer survivors face a range of chronic conditions with functional declines (11, 12) and they are presented with a real threat of secondary cancer (13), with many unmet needs (14). Cancer survivors often are doubtful if exercises are safe during and even after treatment. Is physical activity effective for people who are already weak from cancer treatment? Over two decades of research have revealed that breast cancer patients (and colon, prostate, hematological malignancies) (15, 16) can gain from physical activity programs (17). There is now convincing evidence that post-diagnosis physical activity reduces the risk of cancer recurrence, and other chronic condition. It also contributes to longer survivorship period – especially for breast, colorectal and cervix cancer (11, 12, 18). However, the lifestyles of most people today are more sedentary than active.

Increasing evidence is indicating that cancer survivors can and should engage in physical activity as the efficacy and safety of interventions commenced both during and following cancer treatment have been proven (19-23). Adherence to healthy lifestyle behaviors such as being physically active plays a critical role in cancer prevention as it modifies breast cancer risk in postmenopausal women (24, 25). Breast cancer survivors who adhered to the current physical activity guidelines of 150 minutes/week of moderate-level activity, when compared with those who had low activity, are associated with significantly lower risk of death (RR/HR from 0.58 to 0.71) (26); and no activity (RR/HR=0.36) (27). After a breast cancer diagnosis, a 40% -50% lower risks of mortality has been associated with about 2 to 3 hours of moderate-intensity activity (18, 28), whilst another study indicated a duration of 3 to 5 hours per week. The evidence is strong that exercise before and after breast cancer diagnosis is inversely associated with the risk of recurrence and death (29). Controlling cancer via lifestyle factor such as adopting an active lifestyle is becoming particularly essential in cancer survivor populations.

The recommended PA for general and cancer population

The general exercise recommendation for people undertaking or having completed cancer treatment is low to moderate intensity, regular frequency (3 to 5 times per week) for at least 30 minutes per session (21, 30). This is consistent with recommendations for the general adult population (31). The American College of Sports Medicine (ACSM) recommends that healthy adults (32) and cancer survivors (33) perform a minimum of 30-min moderate-intensity exercise on 5 days/week, for health promotion, whilst the World Cancer Research Fund (WCRF) and the American Institute for Cancer Research (AICR) advocate

a higher dosage to specifically reduce cancer risk: 60 min of moderate-intensity or 30 min of vigorous-intensity exercise, daily (34).

Physical activity for colon cancer

There is convincing evidence that links physical activity with colon cancer. Evidence-based studies had proposed several mechanisms for the role of physical activity in reducing colon cancer risk which includes reduced insulin resistance and hyperinsulinemia, anti-inflammatory action, direct immune action, decreased intestinal transit time or higher vitamin D levels (35). A cohort of 573 women diagnosed with stages I-III colorectal cancer who participated in the Nurses' Health Study, reported women who are most physically active experienced 61% reduced colorectal cancer-specific mortality and 57% reduced overall mortality compared to inactive women (36). A meta-analysis conducted in 2009 on physical activity and colon cancer reported an overall risk reduction of approximately 24% (37) for both men and women.

Physical activity for breast cancer

There are increasing published data to date to show that physical activity has an important preventive role in breast cancer risk. A recent meta-analysis concluded that physical activity before pre-diagnosis reduced all-cause mortality by 18% and physical activity post-diagnosis reduced breast cancer deaths by 24%, all-cause mortality by 41% and disease recurrence by 24% (38). Pronk et al (39) suggested that breast cancer risk was lower for women who spent shorter period on occupational sitting time and for post-menopausal women who exercise at or above the recommended physical activity level which is 30 minutes a day for three to five days at moderate-level of intensity. However, our study showed that most survivors are engaged in predominantly low-moderate physical activity (40).

Physical inactivity during cancer survivorship

Many cancer survivors are not pursuing healthy lifestyle. Despite the known benefits of exercise, only a few older adults reported performing regular exercise (41). A large study by American cancer Society found that only 30 percent to 47 percent (n=9105) met the recommendation for physical activity (42). Today, sedentary behavior has been identified as one of the leading preventable causes of death (43). With increasing cancer burden, the challenge in the global cancer control is to improve understanding between the modifiable determinants of PA and to translate this knowledge into practical actions for a general public health. Therefore, researchers should not be focusing on just physical activity engagement, but also on physical inactivity or sedentary behavior which is now an independent factor regardless of whether women fulfill the recommended guidelines (26, 27).

Specific Benefits of Physical Activity intervention

Research evidence showed that physical activity during and after completion of treatment have resulted in better quality of life (44-46) and even improves fatigue body esteem and mood (47, 48). Epidemiologic studies suggest benefits of physical activity in tackling obesity, a known cancer risk factor, with a strong inverse relationship for breast cancer, especially among post-menopausal women (49). Nevertheless, physical activity engagement is beneficial for both pre-menopausal and post-menopausal women, whereby a 30% to 40% reduction in risk of developing breast cancer is postulated when compared with sedentary women (50).

Research evidence suggests that changes in activity from pre to post-diagnosis influences survival. Thus, intervention to increase an uptake of physical activity engagement post cancer is beneficial and therapeutic during the survivorship period. Survivors with a reduction of moderate-level physical activity by an hour or more per week have a risk of death up to four-fold (27). Among women with breast cancer, and compared to those who were inactive before and after diagnosis, those who increased their activity by about 60 minutes/week or more of moderate-level activity, halved their risk of breast-cancer death, as well as all-cause mortality, compared with those who had no change.

Overall, outcomes from physical activity interventions implemented during cancer survivorship periods suggest a much better adjustment to illness. Potential benefits in health promotion such as cardio-respiratory fitness; muscle mass and bone health; immune function; strength and flexibility; body image; self-esteem and mood. At least three prospective cohort studies on cancer survival have presented evidence of a significant relationship between increased physical activities and reduce mortality (26-28). More than 70 published experimental trials on physical activity for cancer survivors have shown that increased physical activity reduces mortality and the evidence is strongest for breast and colorectal cancers (19, 20, 31) and prostate cancers (51). A large-scale randomized control trial with colorectal survivor via telephone sessions to enable symptom management, psychosocial and lifestyle support, showed promising results which included better quality of life; better diet uptake, and a reduced sedentary behavior (52). Regular, sufficient physical exercise apart from weight maintenance, diet and emotional strategies that may improve wellbeing, quality of life have the potential to reduce the risk of cancer recurrence (53).

Future direction – Cancer survivorship research and practices

There is a need to improve awareness of the needs of adopting low-risk lifestyle changes for cancer survivors and to recognize survivorship needs. Opportunities exist for occupational therapists, oncologists and primary care physicians to collaborate and to promote lifestyle changes

(research and clinical practice) to improve the length and quality of life of their patients.

Theory-driven research studies

Theoretically driven studies, eg the use of social cognitive theory implicating its central tenet variables such as like attitudes and efficacy, help explain the reason for a successful behavior. More theory driven interventions should be used in physical activity behavior-change study. These approaches need to be incorporated into routine clinical care (54-56). Theory-led studies can inform the design of interventions to ensure how best to promote positive attitudes towards healthy behavior and thus enabling long-term behavioral change. Future work needs to assess more thoroughly what constitutes optimal exercise prescriptions, including the mode of delivery, cost effectiveness, frequency, duration, intensity and type, and how individual characteristics (eg. age, cancer type, treatment, presence of specific symptoms) affect this prescription (21). Also, research to find out the optimal period of utilizing these 'teachable moments' are imperative for a successful healthy behavioral lifestyle changes, as well as more rigorous designs which address methodological limitations (57). Occupational therapy studies contribute to lifestyle research to improve the understanding of lifestyle characteristics (eg. activity engagement and coping behaviors) and its relationships to health promotion and disease prevention (58). A recent systematic review (four primary prevention and five tertiary prevention trials) concluded small to moderate effect on improving concentrations of several blood biomarkers implicated in breast and colon cancer pathways (59). More studies are needed explaining the role of physical activity and cancer etiology (primary prevention) and also cancer prognosis (tertiary prevention).

Evidence based clinical practices

In particular, clinicians need to capture and optimize the period(s) of 'teachable moments' for the promotion and the adoption of low-risk lifestyle intervention in cancer care. Along with research evidence, behavioral strategies (such as counseling, coaching, motivational interviewing, goal setting, action planning) across a range of settings during this cancer survivorship period are required to propel cancer survivors to redesign their lifestyle. Specifically for physical activity as a modifiable cancer control factor - the adoption of physical activity as a key index to a healthy lifestyle behaviors must be supported and facilitated.

Conclusion

In conclusion, to quote the pancreatic cancer patient cited above: When persuaded by his wife to engage in more physical activity, he defended and debated with the analogy that the huge healthy oak tree outside his garden is and has been 'sedentary' for decades, but yet, it remains strong and healthy. Most people find it easier to be sedentary than to be active, and thus, the momentum to fight inertia and inactivity does require a strong motive and does need to be supported and reinforced. More health organizational effort is needed if we are to target towards getting cancer survivors to self manage a more active lifestyle. These efforts need organizational commitment, policy commitments, resources and facilities to ensure the Union International for Cancer Control (UICC)'s agenda can be achieved. Lastly, with a steep rise of cancer patients surviving more than five years beyond diagnosis, health systems throughout the world are challenged to expand their focus from acute care to managing this long-term health consequences of cancer. Consolidated, proactive effort for low-risk behaviors amongst cancer survivors must be carefully planned and implemented objective for cancer survivorship. More effort is needed to get cancer survivors to self manage an active lifestyle, and teachable moments must be optimize in order to gain effective engagement and adoption of healthy behaviors. These efforts must be supported by organizational commitment, resources and facilities to ensure this target of cancer control can be delivered to the increasing rise of cancer survivors.

References

1. Hewitt, M., & Ganz, P. A. (2006). *From cancer patient to cancer survivor - Lost in transition: An american society of clinical oncology and institute of medicine symposium*. Washington, D.C.: Institute of Medicine and National Research Council of the National Academies. (T. N. A. Press o. Document Number)
2. Bower, J., Meyerowitz, B., Desmond, K., Bernaards, C., Rowland, J., & Ganz, P. (2005). Perceptions of positive meaning and vulnerability following breast cancer: predictors and outcomes among long-term breast cancer survivors. *Ann Behav Med, 29*(3), 236-245.
3. Jemal, A., Murray, T., Ward, E., Samuels, A., Tiwari, R., Ghafoor, A., et al. (2005). Cancer statistics. *CA Cancer J Clin, 55*, 10-30.
4. Loh, S. Y., & CH Yip. (2006). Breast cancer as a chronic illness: Implication for Rehabilitation and Medical Education. *Jornal of University Malaya Medical Centre, 9*(2), 3-11.
5. Fallowfield, L. (2004). Evolution of breast cancer treatments: current options and quality-of-life considerations. *European Journal of Oncology Nursing (2004) 8S, S75-S82*.
6. Anand, P., Kunnumakara, A. B., Sundaram, C., Harikumar, K. B., Tharakan, S. T., Lai, O. S., et al. (2008). Cancer is a preventable disease that requires major lifestyle changes. *Pharmaceutical Research* 2008; 25(9): 2097-2116.
7. Wendy Demark-Wahnefried, Noreen M. Aziz, Julia H. Rowland, & Bernardine M. Pinto. Riding the Crest of the Teachable Moment: Promoting Long-Term Health After the Diagnosis of Cancer *Journal of Clinical Oncology* 2005; 23(24 (August 20)): 5814-5830.

8. McCarthy, A. M., & Visvanathan, K. (2010). Breast cancer prognosis: weighing the evidence on weight and physical activity. *Oncology, 24*(4), 1-5.
9. World Health Organization. Fact sheet no. 297: Cancer. 2009 [Electronic Version]. Retrieved June 3 2009, from http://www.who.int/mediacentre/factsheets/fs297/en/index.html.
10. Stuart, K., Brennan, B., French, J., Houssami, N., & Boyages, J. Life after breast cancer. *Australian Family Physician* 2006; 35(April 2006): 177-258.
11. Eakin, E. G., Youlden, D. R., Baade, P. D., Lawler, S. P., Reeves, M. M., Heyworth, J. S., et al. (2006). Health Status of Long-term Cancer Survivors: Results from an Australian Population-Based Sample. *Cancer Epidemiology Biomarkers & Prevention, 15*(10), 1969-1976.
12. Hawkes, A., Lynch, B., Youlden, D., Owen, N., & Aitken, J. (2008). Health behaviors of Australian colorectal cancer survivors, compared with noncancer population controls. *Supportive Care in Cancer, 16*(10), 1097-1104.
13. Coory, M., Baade, P., Aitken, J., Smithers, M., McLeod, G., & Ring, I. (2006). Trends for in situ and Invasive Melanoma in Queensland, Australia, 1982–2002 *Cancer Causes and Control, 17*(1), 21-27.
14. Loh, S. Y., Packer, T., Yip, C. H., & Low, W. Y. (2007). Perceived Barriers to Self Management in Malaysian Women. *Asia Pacific Journal of Public Health, 19*(3).
15. Speck, R., Courneya, K. S., Masse, L., Duval, S., & Schmitz, K. An update of controlled physical activity trials in cancer survivors: a systematic review and meta-analysis. *Journal of Cancer Survivorship* 2010; 4(2): 87-100.
16. Velthuis, M. J., Agasi-Idenburg, S. C., Aufdemkampe, G., & Wittink, H. M. The Effect of Physical Exercise on Cancer-related Fatigue during Cancer Treatment: a Meta-analysis of Randomised Controlled Trials. *Clinical oncology (Royal College of Radiologists (Great Britain))* 2010; 22(3): 208-221.
17. Wiskemann, J., & Huber, G. Physical exercise as adjuvant therapy for patients undergoing hematopoietic stem cell transplantation. *Bone Marrow Transplant* 2007; 41(4): 321-329.
18. Holmes, M. D., Chen, W. Y., Feskanich, D., Kroenke, C. H., & Colditz, G. A. (2005). Physical Activity and Survival After Breast Cancer Diagnosis. *JAMA, 293*(20), 2479-2486.
19. Courney, K. S. (2003). Exercise in cancer survivors: an overview of research. *Med Sci Sports Exerc, 35*(11), 1846 - 1852.
20. Galvao, D. A., & Newton, R. U. (2005). Review of exercise intervention studies in cancer patients. *J Clin Oncol, 23*(4), 899 - 909.
21. Hayes, S. C., Spence, R. R., GalvÃ£o, D. A., & Newtonc, R. U. (2009). Australian Association for Exercise and Sport Science position stand: Optimising cancer outcomes through exercise. *Journal of science and medicine in sport / Sports Medicine Australia, 12*(4), 428-434.
22. Monninkhof, E. M., Elias, S. G., Vlems, F. A., van der Tweel, I., Schuit, A. J., Voskuil, D. W., et al. (2007). Physical activity and breast cancer: a systematic review. *Epidemiology, 18*(1), 137-157.
23. Stevinson, Clare, Lawlor, Debbie, A., Fox, & Kenneth, R. Exercise interventions for cancer. *Dordrecht, PAYS-BAS: Springer* 2004; (Vol. 15).
24. Carpenter, C. L., Ross, R. K., Paganini-Hill, A., & Bernstein, L. (2003). Effect of family history, obesity and exercise on breast cancer risk among postmenopausal women. *INTERNATIONAL JOURNAL OF CANCER, 106*(1), 96-102.
25. Gramling, R., Lash, T., Rothman, K., Cabral, H., Silliman, R., Roberts, M., et al. (2010). Family history of later-onset breast cancer, breast healthy behavior and invasive breast cancer among postmenopausal women: a cohort study. *Breast Cancer Research, 12*(5), R82.
26. Kroenke, C., Chen, B., Kawachi, I., Colditz, G., & Holmes, M. (2004). Functional Impact of Breast Cancer by Age at Diagnosis. *JOURNAL OF CLINICAL ONCOLOGY, 22*(10 (May 15)), 1849-1856.
27. Irwin, M. L., Smith, A. W., McTiernan, A., Ballard-Barbash, R., Cronin, K., Gilliland, F. D., et al. (2008). Influence of pre- and postdiagnosis physical activity on mortality in breast cancer survivors: The health, eating, activity and lifestyle study. *Journal of Clinical Oncology, 26*(24), 3958-3964.
28. Holick, C. N., Newcomb, P. A., Trentham-Dietz, A., Titus-Ernstoff, L., Bersch, A. J., Stampfer, M. J., et al. (2008). Physical Activity and Survival after Diagnosis of Invasive Breast Cancer. *Cancer Epidemiology Biomarkers & Prevention, 17*(2), 379-386.
29. Verloop, J., Rookus, M. A., van der Kooy, K., & van Leeuwen, F. E. Physical Activity and Breast Cancer Risk in Women Aged 20-54 Years. *Journal of the National Cancer Institute* 2000; 92(2): 128-135.
30. Ainsworth, B. E. (2009). How do I measure physical activity in my patients? Questionnaires and objective methods. *British Journal of Sports Medicine* 2009; 43(1): 6-9.
31. Courneya, K. S., Mackey, J. R., & McKenzie, D. C. (2002). Exercise for breast cancer survivors: research evidence and clinical guidelines. *30*, 33-42.
32. Haskell, W. L., Lee, I. M., Pate, R. R., Powell, K. E., Blair, S. N., Franklin, B. A., et al. (2007). Physical activity and public health. Updated recommendations for adults from the American College of Sports Medicine and the American Heart Association. *Circulation, 116*, 1081 - 1093.
33. Schmitz KH, Courneya KS, Matthews C, Demark-Wahnefried W, Galvao DA, BM, P., et al. American College of Sports Medicine roundtable on exercise guidelines for cancer survivors. . *Med Sci Sport Exerc* 2010; 42: 1409–1426
34. World Cancer Research Fund, & American Institute for Cancer Research. The second expert report: food, nutrition, physical activity and the prevention of cancer: a global perspective. 2007 [Electronic Version],

35. Wolin, K. Y., Lee, I. M., Colditz, G. A., Glynn, R. J., Fuchs, C., & Giovannucci, E. Leisure-time physical activity patterns and risk of colon cancer in women. *INTERNATIONAL JOURNAL OF CANCER* 2007; 121(12): 2776-2781.
36. Meyerhardt, J. A., Giovannucci, E. L., Holmes, M. D., Chan, A. T., Chan, J. A., Colditz, G. A., et al. (2006). Physical Activity and Survival After Colorectal Cancer Diagnosis. *Journal of Clinical Oncology, 24*(22), 3527-3534.
37. Wolin, K. Y., Yan, Y., Colditz, G. A., & Lee, I. M. Physical activity and colon cancer prevention: a meta-analysis. *British Journal of Cancer* 2009; 100(4): 611-616.
38. Ibrahim, E., & Al-Homaidh, A. (2011). Physical activity and survival after breast cancer diagnosis: meta-analysis of published studies. *Medical Oncology, 28*(3), 753-765.
39. Pronk, A., Ji, B. T., Shu, X. O., Chow, W. H., Xue, S., Yang, G., et al. Physical activity and breast cancer risk in Chinese women. *Br J Cancer* 2011.
40. SY, L., SL, C., & SY, L. Barriers to exercise - Perspectives from multiethnic Cancer survivors. *JUMMEC* 2011; 12(1).
41. Hirvensalo, M., Lampinen, P., & Rantanen, T. (1998). Physical exercise in old age: an eight-year follow-up study on involvement, motives and obstacles among persons aged 65-84 year. *Journal of Aging and Physical Activity, 6*, 157-168.
42. Blanchard, C., Courneya, K., & Stein, K. (2008). American Cancer Society's SCS-II. Cancer survivors'adherence to lifestyle behavior recommendations and associations with health-related quality of life. *J Clin Oncol* 2008: 26(13); 2198-2204.
43. Mokdad, A. H., Marks, J. S., Stroup, D. F., & Gerberding, J. L. (2004). Actual Causes of Death in the United States, 2000. *JAMA, 291*(10), 1238-1245.
44. McNeely, M., Campbell, K., Rowe, B., Klassen, T., Mackey, J., & Courneya, K. (2006). Effects of exercise on breast cancer patients and survivors: a systematic review and meta-analysis. *Med. Assoc. J., 175(1)*, 34-41.
45. Milne, H. M., Gordon, S., Guilfoyle, A., Wallman, K. E., & Courneya, K. S. (2007). Association between physical activity and quality of life among Western Australian breast cancer survivors. *Psycho-Oncology, 16*(12), 1059-1068.
46. Mock, V., Frangakis, C., Davidson, N. E., Ropka, M. E., Pickett, M., Poniatowski, B., et al. (2005). Exercise manages fatigue during breast cancer treatment: A randomized controlled trial. *Psycho-Oncology, 14*(6), 464-477.
47. Pinto, B. M., & Maruyama, N. C. (1999). Exercise in the rehabilitation of breast cancer survivors. *Psycho-Oncology, 8*(3), 191-206.
48. Pinto, B. M., & Trunzo, J. J. (2004). Body Esteem and Mood Among Sedentary and Active Breast Cancer Survivors. *Mayo Clinic Proceedings, 79*(2), 181-186.
49. Monninkhof EM, Elias SG, Vlems FA, & al., e. (2007). Physical activity and breast cancer: a systematic review. . *Epidemiology 18*, 137–157.
50. Thune, I., & Furberg, A.-S. Physical activity and cancer risk: dose-response and cancer, all sites and site-specific. *Medicine & Science in Sports & Exercise* 2001; 33(6): S530-S550.
51. Segal, R. J., Reid, R. D., Courneya, K. S., Sigal, R. J., Kenny, G. P., Prud'Homme, D. G., et al. Randomized Controlled Trial of Resistance or Aerobic Exercise in Men Receiving Radiation Therapy for Prostate Cancer. *Journal of Clinical Oncology* 2009; 27(3): 344-351.
52. Hawkes, A., Gollschewski, S., Lynch, B., & Chambers, S. (2009). A telephone-delivered lifestyle intervention for colorectal cancer survivors 'CanChange': a pilot study. *Psycho-Oncology, 18*(4), 449-455.
53. Demark-Wahnefried, W., Pinto, B., & Gritz, E. (2006). Promoting Health and Physical Function Among Cancer Survivors: Potential for Prevention and Questions That Remain. *J Clin Oncol, 24*(32), 5125-5131.
54. Courneya, K. S., & McAuley, E. (1996). Understanding Intentions to Exercise Following a Structured Exercise Program: An Attributional Perspective1. *Journal of Applied Social Psychology, 26*(8), 670-685.
55. Hausenblas, H. A., Carron, A. V., & Mack, D. E. (1997). Application of the theories of reasoned action and planned behavior to exercise behavior: a meta-analysis. *Journal of Sports & Exercise Psychology, 19*(1), 36-51.
56. Vallance, J. K., Courneya, K. S., Taylor, L. M., Plotnikoff, R. C., & Mackey, J. R. Development and Evaluation of a Theory-Based Physical Activity Guidebook for Breast Cancer Survivors. *Health Education & Behavior* 2008; 35(2): 174-189.
57. Rosalind, R. S., Kristiann, C. H., & Wendy, J. B. Exercise and cancer rehabilitation: A systematic review. *Cancer Treatment Reviews* 2010; 36 : 185–194.
58. Christensen, C., & Baum, M. (Eds.). (2005). *Occupational Therapy: performance, participation and wellbeing*. Thorofare, NJ: SLACK.
59. BM. Winzer, DC. Whiteman, MM. Reeves, & JD. Paratz. (2011). Physical activity and cancer prevention: a systematic review of clinical trials. *Cancer Causes Control* 2011; 22: 811–826.

LEISHMANIASIS IN SOUTHEAST ASIA: THE STORY OF THE EMERGENCE OF AN IMPORTED INFECTION IN A NON-ENDEMIC AREA OF THE WORLD

Viroj W

Visiting University Professor, Hainan Medical University, China

Correspondence:

Professor Viroj Wiwanitkit
Wiwanitkit House, Bangkhae, Bangkok Thailand 10160
Email : wviroj@yahoo.com
Phone : 6624132436

ABSTRACT

Leishmaniasis is a recognized medical condition which, although uncommon, results in early patient mortality. It is however fortunate that such condition is treatable if detected early. Although this condition is mainly found in many Middle Eastern countries, other parts of the world may still be affected largely due to large population migration and ease of travel made possible by modern transportations. It is therefore of paramount importance that such a condition be recognized by health providers because early detection may help to prevent early fatality. In this article, a brief summary of leishmaniasis in Southeast Asia is discussed and how at one time, this condition which was thought to be irrelevant to this part of the world may again emerge as a common medical condition. The article aims to make the readers aware of the existence of this disease and that this disease should be considered as a probable diagnosis since its early identification can lead to better cure rates.

Keywords**:** *bone marrow, leishmaniasis, Southeast Asia*

Introduction

Leishmaniasis, a blood parasitic infection caused by the protozoa *Leishmania spp.* is a fairly common disease in many parts of the underdeveloped and developing countries that infects humans specifically and results in the clinical condition known as leishmaniasis. Leishmaniasis spp. is a Trypanosomatid protozoa and is transmitted through several identifiable vectors. These includes human vectors and animals; in particularly canines (1-3). Other vectors that are responsible for transmitting this disease, includes sandflies (genus Phlebotomus in the Old World and genus Lutzomyia in the New World) (1, 2). Leishmaniasis can be present in two main forms: cutaneous and visceral. The clinical signs and symptoms of leishmaniasis can appear within weeks to months after being inoculated with this parasite (1, 2).

Cutaneous leishmaniasis (CL) manifests as a painless and non-pruritus erythematous papule that further evolves into a plaque or ulcer (1, 2). Spontaneous healing within 2 months to 1 year is possible. However, this will leave scarring and pigmentation changes on the afflicted patients (1, 2). While the disease itself is not difficult to be identified, several differential diagnoses must also be considered since they may have overlapping signs and symptoms. This may include sporotrichosis, blastomycosis, yaw, tuberculosis, leprosy, cutaneous lymphoma, histoplasmosis and penicilliosos (1, 2). For treatment, oral miltefosine has been shown to be the new effective drug acting primarily against this parasite. The use of antibiotic can be applied in cases where secondary bacterial infection has occurred. While cutaneous leishmaniasis is not usually fatal, visceral leishmaniasis on the other hand can be more severe and results in patient mortality. Fever, weight loss, hepatosplenomegaly, pancytopenia and hypergammaglobulinemia are classical characteristics which by itself cannot be distinguished from many other infections (1, 2). Thus a high degree of suspicion of the presence of this disease must be made when such symptoms develop. More importantly, visceral leishmaniasis (VL) affects the liver, spleen and bone marrow and thus treating physician must be aware of its fatal consequences if such conditions are not recognised and treated early. In many cases, amphotericin B is effective in treating this condition although resistance to this drug has been previously demonstrated. In these cases, the use of miltefosine should be considered. However, in cases that involves the reticuloendothelial system (spleen and

liver), with or without bone marrow involvement such drugs may no longer be adequate. Patients will develop severe symptoms presenting with extensive hematological abnormalities. Fortunately, such entities represent only one - tenth of all visceral leishmaniasis cases thus sparing many patients from eventual mortality, although there is no specific treatment being mentioned in any known medical literatures. VL is endemic in the Middle East and South Asia and traditionally, this condition is confined within this region only. However, with the advances of modern transportation, this disease is no longer restricted in its ability to spread. This poses major concerns since this entity is unexpected in non-endemic countries; thus allowing VL to continue being undetected. Such disease becomes undertreated and is now allowed to spread within its new found population over time.

Another form of leishmaniasis, known as bone marrow leishmaniasis (BML), is more commonly seen in immunocompromised hosts. This form of leishmaniasis has become an issue today since the number of immunocompromised population has increased tremendously over recent years (3). Fortunately, although the disease can appear to be severe, it is treatable using existing drugs. BML is endemic in the Middle East but remain prevalent in South Asia and Mediterranian countries, which geographically are neighbouring states. As with any other infectious disease, its spread is no longer restricted thanks to the availability of modern travelling. Considering that leishmaniasis is no longer a disease of a specific region, the present article aims to highlight the pattern of spread of this emerging disease in Asia (Figure 1) and what can be expected in the near future. The realization of the existence of this disease is of importance since it is no longer considered exotic in areas which was once considered as safe heavens.

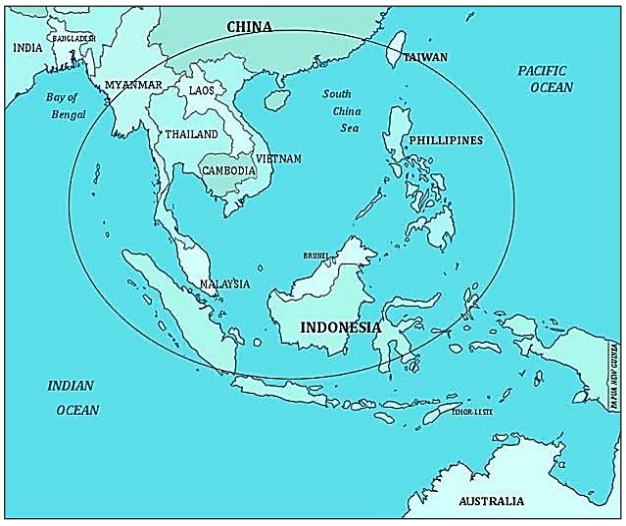


Figure 1: *Map showing Southeast Asia (The area in the circle).*

Leishmaniasis: Cases Reported in Southeast Asia

There have only been a few sporadic case reports of BML in Thailand (3-7). In all cases, disease is detected following a brief patient visit to the Middle East (4-9). Patients develop classical signs and symptoms of the disease which includes fever, weight loss and pancytopenia. The disease was initially diagnosed with difficulty as treating doctor were less receptive of such conditions in Asia. However, bone marrow aspirations following the investigation of unexplained pancytopenia provided undeniable diagnosis of this condition. Once confirmed, treatment was relatively easy with the use of pentavalent antimony compound therapy (1, 2). Ever since these cases were reported, there were no other reports of this disease in Thailand, owing to the decrease in labor emigration then.

Leishmaniasis is considered an important emerging infectious disease in Malaysia. Unlike its northern neighbor, new cases were not reported from its population but rather from their immigrant workers (10, 11). For example, the first case report was of a man from Bangladesh who worked in Malaysia as a laborer (10). A case of VL was also reported in remote areas of Malaysia where immigrant workers have been eluding public authorities for some time. It has been reported that several local people were infected from these workers. The sand-fly, genus Phlebotomus could have played a role in this disease transmission but needed to be further investigated as there is no clear evidence that this appears to be the case. Singapore, like Malaysia also reported several cases of VL affecting their migrant workers (13-15). What may be of interest is the fact that their local population are not spared, and vectors that are traditionally know to contribute to the transmission of this disease has never been identified. There have been reports that Singaporean visiting countries in the Middle East have returned to their home country with leishmaniasis (16).

Reports of leishmaniasis from other Southeast Asian countries is somewhat under reported, mainly due to the unavailability of a system of reporting. This is unfortunate since countries such as Myanmar would have had greater exposure owing to their close proximity to endemic countries. The only countries that has reported VL and BML appear to come from Vietnam (17); which in our opinion is also under reported.

Discussion

Leishmaniasis should be considered a new emerging infective disease that must be given due attention in Southeast Asia (Figure 2) as the number reported appear to be increasing (Table 1). The main factor leading to the rise in the transmission of this disease is the increased rate of travelling of people to the endemic countries and the migration of immigrants from the endemic areas. Most cases are imported cases confirming the nature of this

imported infection in travel medicine aspect in Southeast Asia. Because of its source of origin appears similar to that of the case observed in endemic areas where the disease originates, signs and symptoms reported previously should be applicable to that observed in non-endemic areas. To date, there is still no report of continuous transmission of disease from imported index case to the others and what is more is that there is still no confirmation on the possibility of local vector responsible for the transmission of this disease (15). It is however apparent that due to globalization, physicians in the Southeast Asia region should pay special attention to the possibility of the presence of this disease. Of interest, despite the emergence of this disease, there are still no specific public health policies and practices to deal with this new threat, which in this author's view is indeed very worrying. Local authorities should be made aware of these diseases and make the necessary provisions to ensure that this disease do not become so wide spread that non-endemic countries will now have to combat this disease in a nationwide scale.

Table 1: *A summary of reported cases of bone marrow leishmaniasis in Southeast Asian countries.*

Countries	Reported cases
Brunei	No report
Cambodia	No report
East Timor	No report
Indonesia	No report
Laos	No report
Malaysia	There are some reports in immigrants from the endemic area.
Myanmar	No report
Philippines	No report
Singapore	There are some reports in immigrants from endemic area and Singaporean travelers who visited the endemic countries.
Thailand	There are about 20 case reports in returning Thai workers who had history of labor works in the Middle East. The diagnosis was usually late due to lack of concern of this new emerging disease.
Vietnam	The new emerging case was reported and became the topic for further study on transmission of disease in this region.

Figure 2: *Map of Southeast Asia with corresponding situation of imported cases of bone marrow leishmaniasis*

References

1. Wiwanitkit V, Singh MY. Emerging Infectious Diseases in India. New York: Nova Publisher, 2008.
2. Wiwanitkit V. Bone marrow leishmaniasis: a review of situation in Thailand. *Asian Pac J Trop Med* 2011; 4 (10):757 – 759.
3. Chutaputti A, Siripool P, Chitchang S, Radomyos P. Visceral leishmaniasis (Kala-azar) : with hypersplenism successfully treated with pentavalent antimony: report of 2 cases. *Intern Med* 1986; 2: 262 – 5.
4. Chutaputhi A, Siripool P, Chitchang S, Radomyos P. Visceral leishmaniasis (Kala-azar): a case report. *R Thai Army Med J* 1986; 39: 98 – 5.
5. Seksarn P, Chumdermpadetsuk S, Dharmkrong-At A, Likitnukul S, Mitrakul C, Poshyachinda M. Visceral leishmaniasis: a case report. *Chula Med J* 1984; 28: 1161 – 1170.
6. Tantaterdtham S, Susaengrat W. Visceral leishmaniasis: a case report (from Khon Kaen Regional Hospital). *J Infect Dis Antimicrob Agents* 1991; 8 : 161-163.
7. Suttinont P, Thammanichanont C, Chantarakul N. Visceral leishmaniasis: a case report. *Southeast Asian J Trop Med Public Health* 1987 Mar; 18(1):103-6.
8. Ab Rahman AK, Abdullah FH. Visceral leishmaniasis (kala-azar) and malaria coinfection in an immigrant in the state of Terengganu, Malaysia: A case report. *J Microbiol Immunol Infect* 2011 Jan 13; 44(1):72 – 76. [Epub ahead of print]
9. Hamidah NH, Cheong SK, Abu Hassan J. A case of kala-azar diagnosed by bone marrow aspiration. *Malays J Pathol* 1995 Jun; 17(1):39 – 41.

10. Tan BH, Lam MS, Wong SY. Three new cases of leishmaniasis: implications for the Singapore medical community. *Ann Acad Med Singapore* 1997 Sep; 26(5):717 – 20.
11. Abraham G, Leo YS, Singh M, Wong SY. A case report of visceral leishmaniasis in Singapore. *Ann Acad Med Singapore* 1997 Sep; 26(5):713 – 6.
12. Lew JW, Koh CK, Selvan VS, Shen E. The hunt for an elusive source of pyrexia in a foreign worker. *Singapore Med J* 2007 Apr; 48(4):e111 – 3.
13. Tay HH, Guan R, Kueh YK, Zaman V, Cheah JS. Kala-azar in a Singaporean. *Singapore Med J* 1986 Aug; 27(4):344 – 6.
14. Rosypal AC, Hailemariam S, Wekheye V, Huong LT, Dubey JP, Lindsay DS, Tidwell RR. Survey of dogs from Vietnam for antibodies to visceralizing Leishmania spp. *J Parasitol* 2009 Jun; 95(3):767.
15. Chevalier B, Carmoi T, Sagui E, Carrette P, Petit D, De Mauleon P, Pourriere M, Martinie C, Didier C. Report of the first cases of cutaneous leishmaniasis in East Timor. *Clin Infect Dis* 2000 May; 30(5):840.
16. Stoiser B, Thalhammer F, Chott A, Breyer S, Burgmann H, Graninger W. A case of visceral leishmaniasis in Austria. *Wien Klin Wochenschr* 1998 May 8; 110(9):342 – 5.
17. Joshi DD. Organisation of veterinary public health in the south Asia region. *Rev Sci Tech* 1991 Dec; 10(4):1101 – 29.

AN INTRODUCTION TO PROFESSOR DR HWEE MING CHENG

Prof Hwee Ming Cheng hails from Johor Baru, where he completed his education at St Joseph's Secondary School in 1974. He then crossed the causeway for his pre-university course at the National Junior College in Singapore. Subsequently, he read for his Joint Honours in Medical Cell Biology & Biochemistry at the University of Liverpool, United Kingdom, in 1980 and completed his PhD studies in Liverpool in Immunology in 1983. His PhD research was on the immunobiology of the human placental allograft. After a short post-doctoral stint at the Medical University of South Carolina, USA, Prof Cheng joined the Department of Physiology, Faculty of Medicine, Universiti Malaya in 1985. In 1993, he was promoted to associate professor and ten years later, he became a full professor. His initial research activity in Universiti Malaya was on the physiologic, natural autoantibodies to phospholipids and their possible relationships to autoimmunity in the anti-phospholipid syndrome. Subsequently, Prof Cheng worked on antioxidants in human samples as well as in natural products, in particular palm oil vitamin E. Prof Cheng is a member of the planning committee for the Society for Free Radical Research, Malaysia.

In addition to supervising his postgraduate research students, Prof Cheng has a special interest in understanding how students learn Physiology. Since 2000, he has written more than a dozen Physiology Learning books which incorporate some of the common misconceptions in Physiology among students. His most recent books are *'Thinking through Physiology'* and '*Conceptual Learning in Physiology*' both by Pearson Publishers. Prof Cheng also initiated the Inter-Medical School Physiology Quiz (IMSPQ) in 2003 which is now in its 12th year. The Physiology Quiz is a global stimulus for Physiology education and now draws student teams from more than 70 medical schools from many countries to Universiti Malaya each year. Prof Cheng is a regular examiner in Physiology at the Melaka-Manipal Medical College (Manipal Campus) in India and he is a visiting professor at the Udayana Medical School, Indonesia and Tongji University School of Medicine, Shanghai.

Prof Cheng is married to Dr Gaik Cheng Tan, a medical graduate from the University of Liverpool, and they have been blessed with two children, Timothy (a UM alumnus) who is a houseman in QE Hospital, Kota Kinabalu and Ruth, a Final year medical student in Universiti Malaya.

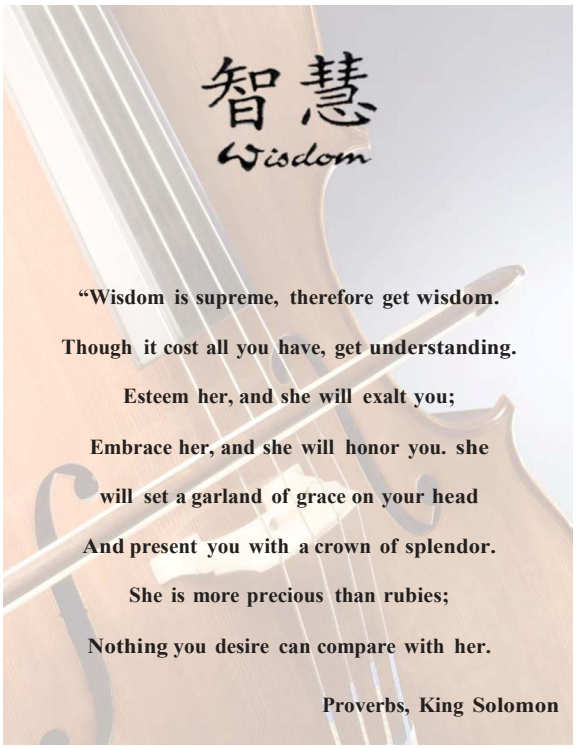
A PHYSIOLOGIC JOURNEY

Cheng HM

Department of Physiology, Faculty of Medicine, University of Malaya, Kuala Lumpur

Correspondence:

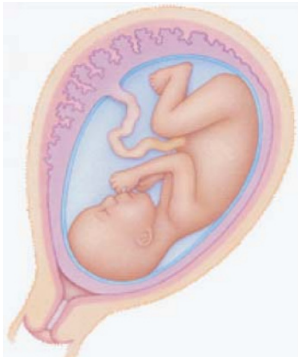
Professor Dr. Cheng Hwee Ming
Department of Physiology
Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur.
E-mail: chenghm@um.edu.my



A Physiologic Journey

"…. You knit me together in my mother's womb".
The Psalmist.

My first systematic introduction to laboratory research began with my post-graduate studies at the Department of Immunology, Royal Liverpool Hospital in 1980. My PhD mentor was Professor Peter Johnson, an inspiring teacher and I learnt much from his approach to addressing research questions and his ability to give meaning to seemingly disjointed data. Peter, as I called him has since retired and happily judges sailing competitions.Above Peter's desk were the words of immunologist, JR Marrack, *"The secret of successful research is to ask nature, simple questions, one at a time".* I was introduced to the mysteries surrounding the natural phenomenon of placental implantation. The placenta, being a 'foreign' fetal allograft, not merely survives passively against any potential maternal immune rejection, but actively provides the nutritive, hormonal and homeostatic lifeline for a relatively long gestation in humans. The placenta is aptly described as 'Nature's Transplant' and research insights into the immunobiology of the successful placental allograft may provide better understanding of how cancer cells avoid host immunosurveillance. I remember my regular visits to the Women's Hospital, Liverpool to collect fresh, still warm samples. The use of a large, easily available human sample has a great advantage as it removes doubts when the relevance of extrapolating animal data to human is concerned. There are obvious expectations that there will be a cross-pollination of knowledge from placental research to human organ transplantation. My PhD involved using monoclonal antibodies produced against the placental syncytiotrophoblast membrane.

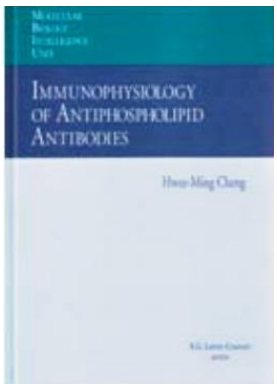


I was proud to publish my first author paper in the journal *Placenta (Cheng HM, Johnson PM. 1985).*

In 1985, on returning home to Malaysia, I joined the Physiology Department then chaired by the late Professor A Raman. There was not a Division of Immunology in the Faculty of Medicine for me to consider applying for. As is the case for many PhDs in the Life Sciences who returned in the early 80's to Malaysian public universities, lack of appropriate research facilities and funds did not permit the continuation of my investigation into the placenta (although of course, the supply of human placentae would not have been a problem!). I subsequently met Prof Yap Sook Fan who was at that time attempting to set up a radio-immunoassay for antibodies to the mitochondrial phospholipid, cardiolipin. The anti-cardiolipin syndrome was beginning to be recognized as a definite autoimmune entity.

"Any kingdom divided against itself will be ruined ….".
Luke the Physician

In the process of testing for anticardiolipin antibodies (aCL) in clinical samples and establishing an enzyme-linked immunoassay (ELISA) for aCL, we serendipitiously observed aCL in normal human sera. This providential finding led to characterization of these physiologic antiphospholipid autoantibodies. The obvious question was the immunological relevance of these natural antibodies in health and disease. At that time, there was progressively accumulating descriptions of natural antibodies to other normal tissue components in the literature. In addition, the natural antibodies are in some cases masked, latent or cryptic and are detectable only when serum components that appear to bind them are removed. Interestingly, the antigenic specificities of these natural antibodies (including aCL) were similar to those found in autoimmune sera. One paradigm shift views the subpopulation of circulating natural antibodies as an essential part of the immunoregulatory network operative in health. In other words, when a specific antibody is detected in e.g. an SLE patient, the presence of that antibody may not necessarily be due to solely a hyperimmune response to antigen. The autoimmune autoantibody could also be exposed and detected when the serum masking factors are reduced, and the cryptic natural antibody with the same specificity then identified by laboratory immunoassays. These studies were satisfying and productive and an invited authorship by a specialty book publisher followed with the release in 1994 of *"Cheng HM, Immunophysiology of Antiphospholipid Antibodies".*



During the course of antiphospholipid investigations, there were some forays into humoral immunity in cancer and in allergy. My friend and scientific colleague, Prof Sam Choon Kook kindly absorbed me into her laboratory team, then at the ENT department under Prof U Prasad. Antibodies to antigens of the Epstein Barr virus (EBV) were of special interest in early screening of the EBV-related nasopharyngeal carcinoma (NPC). Efforts were also made into elucidating the fine linear antigenic epitopes of EBV antigens recognized by antibodies in NPC patients. The aim of such immuno-mapping was to utilize simplified, immunodominant linear peptides in immunoassay for NPC screening.

1997-2010

"Fruit trees of all kinds….will serve for food and their leaves for healing"
Ezekiel the Prophet

In 1997, I spent my Sabbatical at the then Palm Oil Research Institute (now Malaysian Palm Oil Research Board). Dr Kalyana Sundram initiated me into Nutrition research and in particular, the research focus was on palm oil-derived vitamin E. Vitamin E besides its antioxidant properties has other biological actions. Oxidation studies of low-density lipoprotein were carried out and the possible roles of natural antibodies in immunoclearance of oxidized LDL were proposed. Carefully controlled human volunteer projects, including post-prandial studies with different palm vitamin E fractions were also conducted.

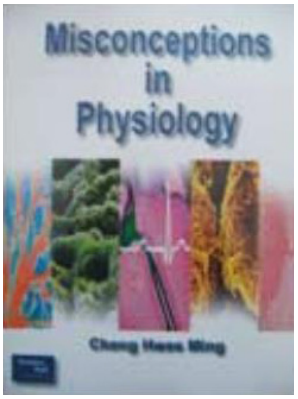
Together with colleagues in SIRIM and International Medical University, we also optimized several tests to screen for net free radical scavenging activities in Malaysian natural products. One surprising finding that was eventually patented was the detection of a high level of antioxidant activity in the uneaten skins of our common rambutan fruit.

An important question relates to the bioavailability of dietary antioxidants. Some investigations in intestinal absorption in rats were carried out using extracts of the Mulberry plant as the antioxidant source. We encountered serendipitiously what might be an important natural antioxidant defence phenomenon in isolated intestinal preparation (unpublished).

In 2003, while enjoying my 3rd Sabbatical, I initiated the 1st Inter-Medical School Physiology Quiz (IMSPQ). From an initial small competition of only 7 national medical schools, the IMSPQ has bloomed and expanded. In the recent 2010 8th IMSPQ, we had 40 medical university teams from 15 countries participating. The IMSPQ is now an annual global gathering of both medical students and lecturers hosted proudly by the Department of Physiology, Universiti Malaya. As Organizing Chairman of the IMSPQ, it has been most fulfilling to be part of the unique gathering of medical students and Physiological educators. The American Physiological Society has recognized this stimulus for encouraging Physiology learning and has invited a write-up of the event in their *"Advances in Physiology Education" journal (Cheng HM, 2010).*

> *"The Teacher searched to find just the right words, ..."*
>
> *Ecclesiastes*

After 15 years of teaching and reading Physiology, it was time to summarize and concretize some of the insights gained from seeing how students learn. It is well said that *'Writing focuses the mind'*. In 2000 I began writing and formulating questions in diverse ways to help students assimilate major Physiological concepts as well as to highlight common misconceptions in integrating Physiological mechanisms in a dynamic subject. Students truly are our best teachers. Tutorial and walk-in questions and answers verbalized by the students provide a window into how they are processing the myriads of information. Even ridiculous answers in examination papers can sometime provide such a gem if one ponders a little. The time spent with and the effort put into listening to students have been enriching. The fruits of this joyful labour are part of the 16 Physiology learning books that have been written.



In describing my 'Physiologic Journey', I decided to list some major milestones along the way. Milestones are often seen as achievements and they are worthy of some praise. Among the milestones on my journey, there are some that are happily beyond my control. Especially are the wonderful gifts of my two children Timothy and Ruth and my friend and companion for life, Gaik Cheng.

The journey continues in the land of Academia...

> *"All their life in Narnia had been the cover and the title page: now at last they were beginning Chapter One of the Great Story which no one on earth has read: which goes on forever: in which every chapter is better than the one before".*
>
> The Last Battle, CS Lewis

The text was presented in an inaugural lecture by Professor Dr. Cheng Hwee Ming in the Faculty of Medicine, University of Malaya on the 1st April 2011.

LIST OF REVIEWERS FOR VOLUME 15, ISSUE 1, 2012

Professor Dr. Cheong Sok Ching

Department of Oral & Maxillofacial Surgery,
Faculty of Dentistry, University of Malaya, Kuala Lumpur

Dr Matin Mellor Abdullah

Subang Jaya Medical Centre,
Shah Alam, Selangor

Associate Prof. Dr. Fauzi M. Anshar

Department of Medicine,
UKM Medical Centre, Cheras, Kuala Lumpur

Associate Prof Dr Pang Yong Kek

Department of Medicine,
Faculty of Medicine, University of Malaya, Kuala Lumpur

Associate Prof. Dr. Veeranoot Nissapatorn

Department of Parasitology,
Faculty of Medicine, University of Malaya, Kuala Lumpur

Professor Dr. Rohela Mahmud

Department of Parasitology,
Faculty of Medicine, University of Malaya