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Avastin has been approved across multiple tumor types: [1-6]

First-line mCRC Superior OS (p<0.001)	30% Increase in median OS
First-line mNSCLC Superior OS (p=0.003)	19% Increase in median OS
Front-line OC Superior PFS (p<0.001)	37% Increase in median PFS
First-line mBC Superior PFS (p<0.0001)	95% Increase in median PFS
First-line mRCC Superior PFS (p=0.0001)	89% Increase in median PFS
Relapsed GBM	6-month PFS: 42.6% ORR: 28.2%

Abbreviated Prescribing Information – Avastin Roche Injection 100mg/4 ml (bevacizumab)

Indications: *Metastatic colorectal cancer (mCRC)* - in combination with fluoropyrimidine-based chemotherapy for treatment of mCRC. *Metastatic breast cancer (mBC)* - in combination with paclitaxel for 1st line treatment of mBC. *Non-small cell lung cancer (NSCLC)* - in addition to platinum-based chemotherapy for 1st line treatment of unresectable, advanced, metastatic or recurrent NSCLC other than predominantly squamous cell histology. *Advanced and/or metastatic renal cell carcinoma (mRCC)* - in combination with interferon alfa-2a for the treatment of mRCC. *Glioblastoma* - for the treatment of glioblastoma with progressive disease following prior therapy as a single agent. *Epithelial ovarian, fallopian tube or primary peritoneal cancer* - in combination with carboplatin and paclitaxel for front-line treatment of advanced (FIGO stage III B, III C & IV) cancer; in combination with carboplatin and gemcitabine for 1st recurrence of platinum-sensitive cancer who have not received prior bevacizumab therapy / other VEGF inhibitors / receptor-targeted agents.

Dosage & Administration: Physicians experienced in antineoplastic medicines should supervise Avastin Roche administration. Continue treatment until progression of underlying disease or unacceptable toxicity (except for Glioblastoma). *mCRC* - 5mg/kg or 10mg/kg every 2 weeks; or 7.5mg/kg or 15mg/kg once every 3 weeks. *mBC* - 10mg/kg every 2 weeks; or 15mg/kg every 3 weeks. *NSCLC* - 7.5mg/kg or 15mg/kg every 3 weeks in addition to platinum-based chemotherapy for up to 6 cycles, then as monotherapy. *mRCC/Glioblastoma* - 10mg/kg once every 2 weeks. *Epithelial ovarian/Fallopian tube/Primary peritoneal cancer – front-line:* 15mg/kg once every 3 weeks in addition to carboplatin and paclitaxel for up to 6 cycles, then as monotherapy; *recurrent disease:* 15mg/kg once every 3 weeks in combination with carboplatin and gemcitabine for 6 cycles and up to 10 cycles, then as monotherapy. Method of administration: *initial dose:* IV infusion over 90 minutes; if initial dose well tolerated, *second dose:* IV infusion over 60 minute; if second dose well tolerated, subsequent doses: IV infusion over 30 minutes. Do not administer as IV push or bolus or mix with glucose. Dose reduction for adverse events not recommended. If indicated, discontinue or temporarily suspend therapy. No recommendations for use in children or adolescents (<18 years old). No dose adjustment in the elderly.

Contraindications: Hypersensitivity to bevacizumab or any of the excipients, Chinese hamster ovary cell products and other recombinant human or humanised antibodies. Pregnancy.

Warnings & Precautions: *Gastrointestinal (GI) perforation:* increased risk for development of GI perforation and gall bladder perforation; intra-abdominal inflammatory process may be a risk factor for GI perforations in patients with metastatic carcinoma of the colon or rectum thus caution is needed; discontinue therapy permanently in patients who develop GI perforation. *Fistulae:* increased risk for development of fistulae; permanently discontinue in tracheoesophageal or any Grade 4 fistula, consider discontinuation in non-GI fistula. *Wound healing:* do not initiate for at least 28 days following major surgery or until surgical wound is fully healed; withhold for elective surgery. *Necrotizing Fasciitis:* cases including fatality has been reported, discontinue therapy in patients who developed necrotizing facitis. *Hypertension:* control pre-existing hypertension prior to initiation. Monitor blood pressure during therapy and control hypertension with standard antihypertensive therapy; the use of diuretics to manage hypertension is not advised in patients on cisplatin-based chemotherapy. Permanently discontinue if medically significant hypertension remains uncontrolled or for hypertensive crisis/encephalopathy. *Posterior Reversible Encephalopathy Syndrome (PRES):* should PRES develops, confirm by brain imaging, treat symptoms and discontinue Avastin Roche. PRES signs include: seizures, headache, altered mental status, visual disturbance or cortical blindness with/without associated hypertension. *Proteinuria:* Patients with a history of hypertension may be at increased risk for the development of proteinuria; monitoring of proteinuria by dipstick urinalysis is recommended prior to starting and during therapy. Therapy should be permanently discontinued if Grade 4 proteinuria is developed. *Arterial thromboembolism:* including cerebrovascular accidents, transient ischaemic attacks and myocardial infarctions, especially if prior history or elderly. Permanently discontinue if arterial thromboembolic events develops. *Venous thromboembolism:* including pulmonary embolism; discontinue in Grade 4 pulmonary embolism and closely monitor where ≤Grade 3. *Haemorrhage,* especially tumour-associated haemorrhage: discontinue permanently if Grade 3/4. Risk of CNS haemorrhage in patients with untreated CNS metastases has not been prospectively evaluated in clinical studies. Patients should be monitored for signs and symptoms of CNS bleeding and discontinue Avastin Roche in cases of intracranial bleeding. Caution in patients with congenital bleeding diathesis, acquired coagulopathy or during anticoagulant therapy. Serious/fatal *pulmonary haemorrhage/haemoptysis* in non-small cell lung cancer: do not use where recent significant pulmonary haemorrhage/haemoptysis (>1/2 teaspoon of red blood). *Congestive Heart Failure (CHF):* caution in patients with clinically significant cardiovascular disease or pre-existing CHF; most of the patients who experienced CHF had metastatic breast cancer and had received previous treatment with anthracyclines, prior radiotherapy to the left chest wall or other risk factors for CHF, such as pre-existing coronary heart disease or concomitant cardiotoxic therapy. *Neutropenia and infections:* fatal infection with or without severe neutropenia in combination with myelotoxic chemotherapy, mainly seen in combination with platinum- or taxane-based therapies in the treatment of NSCLC and mBC. *Hypersensitivity:* Close observation during and following the administration. Infusion should be discontinued and appropriate medical therapies should be administered if a reaction occurs. *Osteonecrosis of the jaw (ONJ):* concomitant treatment with i.v. bisphosphonates and invasive dental procedures are identified risk factors to ONJ; patients who have previously received or are receiving i.v. bisphosphonates should avoid invasive dental procedures, if possible. *Intravitreal use:* Avastin Roche is not formulated for intravitreal use. *Eye disorders:* including endophthalmitis, intraocular inflammation, retinal detachment, retinal pigment epithelial tear, intraocular pressure increased and intraocular haemorrhage have been reported following unapproved intravitreal use of Avastin Roche compounded from vials approved for cancer patients, some reactions results in visual loss. *Systemic effect following intravitreal use:* reduction of VEGF conc. has been demonstrated, non-ocular haemorrhages and ATE has been reported. *Ovarian Failure / Fertility:* Fertility preservation strategies should be discussed with women of child-bearing potential prior treatment.

Drug Interactions: No clinically relevant pharmacokinetic interaction between co-administered chemotherapy and Avastin Roche. Safety and efficacy with concomitant radiotherapy has not been established. Microangiopathic haemolytic anaemia has been reported when Avastin Roche was used with sunitinib malate; hypertension, elevated creatinine and neurological symptoms were also observed. Increased rates of severe neutropenia, febrile neutropenia, or infection with or without severe neutropenia have been observed in patients on platinum- or taxane-based therapies in the treatment of NSCLC and mBC. No interaction studies have been performed between EGFR monoclonal antibody and bevacizumab chemotherapy regimens, decreased PFS/OS and increased toxicity was observed in phase III studies. **Use in Pregnancy & Lactation:** Avastin Roche should not be used during pregnancy because no adequate & well-controlled data in pregnant women. Inhibition of foetal angiogenesis is anticipated. Avastin Roche may have temporary adverse effect on female fertility and cause ovarian failure. Women with childbearing potential must use effective contraception during and for up to 6 months after treatment. Discontinue breast-feeding during treatment and for at least 6 months after last dose.

Undesirable Effects: For full listings please refer to the Avastin Roche package insert. *Most serious reactions:* GI perforation; haemorrhage including pulmonary haemorrhage/haemoptysis and arterial thromboembolism. *Serious reactions, very common:* Febrile neutropenia, leucopenia, thrombocytopenia, neutropenia, peripheral sensory neuropathy, hypertension, diarrhoea, nausea, vomiting, asthenia and fatigue. *Serious reactions, common:* Sepsis, abscess, infection, anaemia, dehydration, cerebrovascular accident, syncope, somnolence, headache, congestive cardiac failure, supraventricular tachycardia, arterial thromboembolism, deep vein thrombosis, haemorrhage, pulmonary embolism, dyspnoea, hypoxia, epistaxis, intestinal perforation and obstruction, ileus, abdominal pain, GI disorder, stomatitis, palmar-plantar erythrodysaesthesia syndrome, muscular weakness, myalgia, arthralgia, proteinuria, urinary tract infection pain, lethargy and mucosal inflammation. *All grades, very common:* Anorexia, dysgeusia, headache, dysarthria, eye disorder, lacrimation increased, hypertension, dyspnoea, epistaxis, rhinitis. constipation, stomatiti s, rectal haemorrhage, diarrhoea, ovarian failure, exfoliative dermatitis, dry skin, skin discolouration, arthralgia, proteinuria, pyrexia, asthenia, pain and mucosal inflammation. *Other reactions:* Hypertensive encephalopathy. PRES (rare). Renal thrombotic Microangiopathy manifested as proteinuria. Nasal septum perforation. Pulmonary hypertension. Dysphonia. GI ulcer. Gall bladder perforation. Hypersensitivity. Necrotizing fasciitis. ONJ. Laboratory abnormalities and Post Marketing – refer to package insert.

Date of preparation: May 2013

Full prescribing information (Current at Apr-2013) should be viewed prior to prescribing.

References:

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AVASTIN Roche® bevacizumab

Leading angiogenesis inhibition

Contents

Announcement

The Federation of Medical Societies of Hong Kong is calling for interested health care providers to offer discounted health and body check programmes to members of our member societies and their family members.

For those who are interested, please contact our secretariat with information of proposed packages and quotations.

Thank you for your kind attention!

Disclaimer

The Cover Shot

Food: hope, hype and hoax?

There are many statements in the media including newspapers, magazines, books, websites and emails addressing issues of food on the preventing and treatment for cancers. Many of these statements are proven wrong and only minority of the remaining are scientifically based and further detailed investigations have to be done before making recommendations to the public.

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Editorial

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Our May issue has covered the highlights in management of breast cancer, lung cancer and Non-Hodgkin Lymphoma. This issue will focus on the updated management in another three commonly seen cancers, namely, colorectal cancer, prostate cancer and nasopharyngeal carcinoma (NPC).

The incidences of both colorectal cancer and prostate cancer are rising rapidly over the last two decades in Hong Kong. Together they account for more than 2,000 cancer deaths every year. At the same time, these two cancers are also the few cancers that cancer screening is possible and practicable. Although we are not yet sure which is the best method, stool occult blood tests, sigmoidoscopy or colonoscopy have been widely recommended as colorectal cancer screening for those aged between 50-75.

On the other hand, debates persist whether the Prostate-surface Antigen (PSA) test should be recommended for prostate cancer screening since it may lead to unnecessary biopsies and over-treatment of indolent non-life-threatening cancers. Whilst the U.S. Preventive Services Task Force and American College of Physicians recently recommended against PSA screening, the American Urological Society and the American Cancer Society still recommend screening for prostate cancer in selected age groups and risk levels. Hence individual discussion of potential risks and benefits are needed before PSA screening.

Nasopharyngeal carcinoma is largely an endemic disease occurring along the coastal region of South China and its incidence has been slowly decreasing over the last decade. Nevertheless it still accounts for more than half of the head and neck cancers seen locally and ranks seventh in the top ten cancer list of 2010. Although the treatment outcome has significantly improved after the introduction of concurrent chemo-irradiation and sophisticated radiotherapy techniques, late-staged patients still suffer substantial treatment complications and mortality. Although there is yet no proven role for mass NPC screening, small retrospective studies suggest that NPC screening (with EBV serology test with or without endoscopy) may be considered in adults with a family history of NPC.

There will also a coverage on effect of food on cancer and nutrition support to cancer patients. We hope this can provide some non-drug aspect of cancer care.

IRESSA™
gefitinib

1st line treatment in EGFR mutation positive advanced NSCLC[1]

AstraZeneca
ONCOLOGY
Putting progress into practice

EGFR = Epidermal Growth Factor Receptor
M+ = Mutation-positive
NSCLC = Non-Small Cell Lung Cancer

Reference
1. IRESSA HK Prescribing Information, Jun 2011

Abbreviated Prescribing Information
Presentation: Gefitinib film-coated tablet. **Indications:** 1) First line treatment of locally advanced or metastatic NSCLC who have activating mutations of the EGFR TK. 2) Treatment of locally advanced or metastatic NSCLC after failure of cytotoxic chemotherapy. Previous therapy should have included a platinum and a taxane. **Dosage:** 250mg once daily. Tablet can be dispersed in half a glass of drinking water (non-carbonated) without crushing it, stir until the tablet is dispersed and drink immediately. The liquid can also be administered through a naso-gastric tube. **Contraindications:** Severe hypersensitivity to any ingredients of this product; Pregnancy & lactation. **Precautions:** EGFR mutation assessment is recommended for first line treatment; Interstitial lung disease; Worsening of respiratory symptoms; Asymptomatic increase in liver transaminases. **Interactions:** CYP3A4 inhibitors e.g. itraconazole, ketoconazole, clotrimazole & ritonavir; CYP3A4 inducers e.g. rifampicin, phenytoin, carbamazepine, barbiturates & St John's wort; Drugs that increase gastric pH; Warfarin; Metoprolol. **Undesirable effects:** Diarrhoea, nausea, vomiting, stomatitis, elevations in alanine aminotransferase, anorexia, rash, asthenia. **Full local prescribing information is available upon request. APLHK.IRE.0611**

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Screening for CA Prostate

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This article has been selected by the Editorial Board of the Hong Kong Medical Diary for participants in the CME programme of the Medical Council of Hong Kong (MCHK) to complete the following self-assessment questions in order to be awarded 1 CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 30 September 2013.

Introduction

Prostate cancer is common. In Hong Kong, it is the third commonest cancer in males; in 2010, there were 1,942 new cases (10.9 % of all cancers) and 319 prostate cancer deaths (4.1% of all cancer deaths). The lifetime risk of a man in Hong Kong to develop prostate cancer is 3.2 percent, but the risk of dying of prostate cancer is only 0.34 percent [1].

Many cases of prostate cancer do not become clinically evident, as indicated in autopsy series, where prostate cancer is detected in one-third of men under the age of 80 and in two-thirds of older men[2].

The five-year survival among men with cancer confined to the prostate (localised) or with just regional spread is close to 100 percent compared with 31.9 percent among those diagnosed with distant metastases[3]. Therefore screening prostate cancer may have a role to identify asymptomatic men with aggressive localised tumours and successfully treat the disease at an early stage to reduce prostate cancer morbidity and mortality.

The use of Prostate-specific antigen (PSA) in screening started about 20 years ago. Since then there were guidelines issued supporting prostate cancer screening with PSA[4]. The dramatic increase in the incidence of prostate cancer doubling the incidence in Hong Kong from 1996 to 2010 is mainly related to the increase of PSA testing during this period. (Figure 2) The unexpected drop in incidence in patients over 75 years old in Hong Kong can also be explained by the decreased use of PSA screening for men over 75. (Figure 1)

Figure 1. The Incidence and Mortality Trends for Prostate Cancer from 1996 to 2010

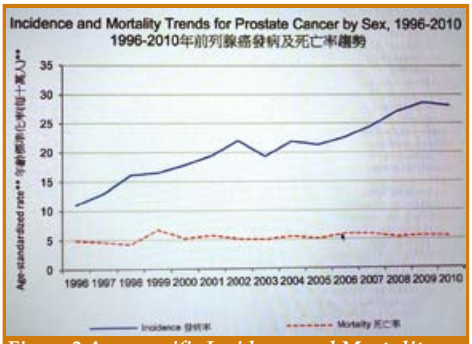

Figure 2 Age-specific Incidence and Mortality Rates for Prostate Cancer in 2010

Contrary to most evidence based medicine practices, prostate cancer screening has adopted PSA testing in the absence of randomised trials.

Prostate-Specific Antigen (PSA)

PSA is a glycoprotein produced by prostate epithelial cells. PSA levels may be elevated when the tissue barriers between the prostate gland lumen and the capillaries are damaged, releasing more PSA into the serum. PSA has a half-life of 2.2 days. PSA elevations can precede clinical manifestation of prostate cancer by 5 to 10 years. It can also be elevated in a number of benign conditions including benign prostatic hyperplasia (BPH), prostatitis, post ejaculations and prostatic biopsy.

Finasteride (Proscar), a 5α- reductase inhibitors can lower PSA levels. The Prostate Cancer Prevention Trial suggests that PSA values would be multiplied by a factor of 2 for the first two years of finasteride therapy, and by 2.5 for longer-term use[5].

Sensitivity and specificity

The traditional cutoff level for an abnormal PSA level in the major screening studies has been 4.0 ng/mL. In a pooled analysis by the American Cancer Society[6], the estimated sensitivity of a PSA cutoff of 4.0 ng/mL was 21 percent for detecting any prostate cancer and 51 percent for detecting high-grade cancers (Gleason ≥8). Lowering the cutoff to 3.0 ng/mL increased these sensitivities to 32 and 68 percent, respectively. The estimated specificity was 91 percent for a PSA cutoff of 4.0 ng/mL and 85 percent for a 3.0 ng/mL cutoff. For men with symptomatic benign prostatic hyperplasia PSA has poorer discriminating ability[7].

Improving the accuracy of PSA

Many methods have been suggested to improve the diagnostic performance of PSA when levels are below 10.0 ng/mL. These include measuring PSA velocity (changes in PSA over time), PSA density (PSA per unit volume of prostate), free PSA, and using age-specific reference ranges. However, none of these add predictive information to the total PSA in randomised trials. For example, a meta-analysis concluded that free-to-total PSA ratio is generally only clinically helpful at extreme values of the ratio[8].

Age-specific reference ranges

PSA levels increase with age, mainly due to a higher prevalence of benign prostatic hyperplasia in the elderly. Some laboratories have used age-specific reference ranges developed from normal populations to improve the PSA[9]:

- 40 to 49 years — 0 to 2.5 ng/mL
- 50 to 59 years — 0 to 3.5 ng/mL
- 60 to 69 years — 0 to 4.5 ng/mL
- 70 to 79 years — 0 to 6.5 ng/mL

Increasing the upper limit for the elderly improves specificity, reducing unnecessary biopsies. Conversely, lowering the threshold in younger men improves sensitivity and increases detection of early-stage tumours. However, a retrospective analysis of a large screening cohort found that the use of age-specific reference standards may miss nearly half of the clinically localised tumours in men over 70 and, more importantly, lead to a 45 percent increase in unnecessary biopsies for men in their fifties.[10] Therefore, the clinical use of age-specific reference ranges is not established, and is not recommended by the US Food and Drug Administration (FDA).

There is no consensus on using any of the PSA modifications, and none of them has been shown in clinical trials to reduce the number of unnecessary biopsies or improve clinical outcomes. The total PSA cutoff of 4.0 ng/mL has been the most accepted standard because it is a tradeoff between missing important cancers at a curable stage and avoiding detection of clinically insignificant disease and subjecting men to unnecessary procedures.

Digital Rectal Examination

Digital Rectal Examination (DRE) can detect induration, asymmetry or nodules but only in the posterior and lateral aspects of the prostate gland. The majority of cancers detected by digital examination alone are clinically or pathologically advanced. No controlled studies have shown a reduction in the morbidity or mortality of prostate cancer when detected by DRE at any age. Thus, the greatest value of DRE may be its use in combination with PSA testing.

Transrectal ultrasonography

Transrectal ultrasonography (TRUS) is not recommended as a primary screening test for prostate cancer because of its low sensitivity and positive predictive value. TRUS is typically used to guide prostatic biopsy rather than as a screening test itself.

Benefit of Screening

The Surveillance Epidemiology and End Results (SEER) tumour registry data have shown a significant decline in the incidence of advanced stage disease and slight reduction of mortality, potentially consistent with effective screening[14]. Strictly speaking this reduction can also be due to more refined surgical and radiotherapy techniques and the use of androgen deprivation therapy and chemotherapies.

Evidence from randomised trials

Two well-designed large randomised trials: the European Randomised Study of Screening for Prostate Cancer (ERSPC) and the United States Prostate, Lung, Colorectal and Ovarian Cancer (PLCO) Screening Trial on screening have shown conflicting results:

In the ERSPC study involving 42,376 men, during a median follow-up of 9 years, the cumulative incidence of prostate cancer was 8.2% in the screening group and 4.8% in the control group. The rate ratio for death from prostate cancer in the screening group, as compared with the control group, was 0.80 (95% confidence interval, 0.65 to 0.98; P=0.04). The absolute risk difference was 0.71 deaths per 1000 men. This means that 1410 men would need to be screened and 48 additional cases of prostate cancer would need to be treated to prevent one death from prostate cancer.[19]

The PLCO study involved ten US centres and 76,693 men and randomised them into a screening group and a control group. After 7 to 10 years of follow-up, the rate of death from prostate cancer was very low and did not differ significantly between the two study groups.[20]

A 2010 meta-analysis summarised the results from six randomised trials (including unique data from two ERSPC sites, with a total of 387,286 participants)[13]. Screening with PSA with or without DRE compared to no screening did not reduce deaths from prostate cancer ([RR] 0.88, 95% CI 0.71-1.09). However, screening significantly increased the probability in the diagnosis of cancer (RR 1.46, CI 1.21-1.77).

In a 2011 Cochrane meta-analysis that had similar findings, the estimated prostate cancer-specific mortality difference was not statistically significant (RR 0.95, 95% CI 0.85-1.07), but cancer was diagnosed significantly more often in men randomised to screening (RR 1.35, 95% CI 1.06-1.72) [18].

Problems Arising from Screening

Risks of biopsy — Prostate biopsies can cause complications (e.g., bleeding, infection) serious enough to require hospitalisation, Hospitalisation rates for infectious complications in these studies have ranged from 0.6 to 4.1 percent[11].

A Canadian study found a 30-day mortality rate of 0.09 percent[12]. Prostate biopsies can also lead to anxiety and physical discomfort.

Over-diagnosis — Over-diagnosis refers to the detection of tumours by screening that would never be clinically significant. Patients may be subjected to the risks of

screening, confirmatory diagnosis, and treatment, as well as suffering potential psychosocial harm from anxiety and labelling. Over-diagnosis is of particular concern because most men with screening-detected prostate cancers have early-stage disease and will be offered aggressive treatment.

In Hong Kong, while the lifetime risk of being diagnosed with prostate cancer has increased to 3.2 %, the lifetime risk of dying from prostate cancer has remained around 0.3% following the advent of PSA testing[1].

Risks of therapy — Even in the absence of treatment, many men found to have prostate cancer as a result of screening will have a lengthy period of time without clinical problems. However, undergoing radical prostatectomy and radiation therapies can lead to immediate complications: The operative mortality rate is about 0.5 percent, though the rate approaches 1 percent in men over 75 years. Less serious, but more common complications include urinary incontinence, sexual dysfunction, and bowel problems. Radical prostatectomy can substantially decrease sexual function in 20 to 70 percent of men and lead to urinary problems in 15 to 50 percent[15].

External beam radiotherapy has been reported to cause erectile dysfunction in 20 to 45 percent of men with previously normal erectile function, urinary incontinence in 2 to 16 percent of previously continent men, and bowel dysfunction in 6 to 25 percent of men with previously normal bowel function[14].

Approach to screening — Although screening for prostate cancer with PSA can reduce mortality, the absolute risk reduction is small. There are important concerns about whether the benefits of screening outweigh the potential harms to quality of life, including the substantial risks for over-diagnosis and treatment complications. There are always men who are willing to accept a substantial risk of morbidity associated with treatment in return for a small reduction in mortality. In general, men who are at increased risk of prostate cancer because of race or family history may be more likely to benefit from screening.

Age to begin screening — Screening should be discussed with men beginning at age 50, but not with men who have co-morbidities that limits their life expectancy to less than 10 years. For high risk men: family history, particularly in relatives younger than age 65, and BRCA1 or BRCA2 mutations carrier may start screening at age 40.

Frequency and method of screening —The optimal interval of PSA alone for screening is still uncertain.

Studies have also raised the possibility of less frequent (up to every 4 years) to retest men with lower initial PSA levels (eg, ≤1.0, 1.5. or 2.0 ng/mL), while still testing annually in those with higher PSA levels (but still below a cutoff for biopsy). [17]

Conclusion

Recommendations from various authorities have been summarised in the following table. Although screening for prostate cancer can reduce mortality from prostate cancer, the absolute risk reduction is very small. Given the limitations in the design and reporting of the randomised trials, there remain important concerns that the benefits of screening are outweighed by the potential harms to quality of life, including the substantial risks for over-diagnosis and treatment complications. Individual patient preferences are to be respected. Men who are expected to live at least 10 years and are old enough to be at significant risk for prostate cancer should be provided with information on the risks and benefits of screening. In general discussion should start at age 50 or at age 40 for men with a positive family history or known to have the BRCA1 mutation. Screening can be performed with Prostate-specific Antigen (PSA) tests at intervals ranging from every two to four years. Digital rectal examination is not recommended as part of screening. When co-morbidities occur or when life expectancy is less than 10 years (e.g. age > 75), screening should be stopped.

Authority	Recommendations	Remarks
American Cancer Society (ACS)	Recommends PSA testing with or without DRE for average-risk men beginning at 50 years of age. Screening should not be offered to men with a life expectancy of less than 10 years	Emphasises the need for involving men in the decision with sufficient information regarding the risks and benefits of screening and treatment provided
American Urological Association (AUA)	Recommends against screening men younger than 40, and also does not recommend routine screening for average-risk men ages 40 to 54, men older than 70, or men with a life expectancy of less than 10 to 15 years.	Decisions should be individualised for higher-risk men ages 40 to 54
United States Preventive Services Task Force (USPSTF)	Recommends against screening for prostate cancer, concluding that there is moderate certainty that the benefits of such screening do not outweigh the harms.	Advise that men requesting screening be supported in making an informed decision..
Canadian Task Force on Preventive Health Care	Recommends against screening for prostate cancer with PSA or TRUS	Insufficient evidence to recommend for or against screening with DRE
United Kingdom National Screening Committee	Not recommend screening for prostate cancer	
Australian Cancer Council	Not support population-based screening	Recommends a patient-centred approach that individualises the decision.
European Society for Medical Oncology (ESMO)	Recommends against population based screening and in favour of anindividualised approach using shared decision making	Inconsistent evidence on screening men younger than 50 and between 70 and 75 years of age, and evidence that the harms of screening outweigh the benefits for men over age 75.
Clinical Guidelines Committee of the American College of Physicians (ACP)	Recommends against screening for prostate cancer in average-risk men under the age of 50 and against screening in men over the age of 69 or with a life expectancy less than 10 to 15 years.	Inform men ages 50 to 69 about the limited potential benefits and substantial harms of prostate cancer screening and only screen men who express a clear preference for being screened

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MCHK CME Programme Self-assessment Questions

Please read the article entitled "Screening for CA Prostate" by Dr. Victor HSUE and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded CME credit under the Programme for returning completed answer sheets via fax (2865 0345) or by mail to the Federation Secretariat on or before 30 September 2013. Answers to questions will be provided in the next issue of The Hong Kong Medical Diary.

Questions 1-10: Please answer T (true) or F (false)

1. Prostate cancer accounts for more than 10 % cancer death in Hong Kong.
2. PSA elevations can precede clinical manifestation of prostate cancer by 5 to 10 years.
3. A free-to-total PSA ratio is clinically very helpful to distinguish benign from malignant prostate onditions.
4. Age-specific reference ranges for PSA are recommended by the US Food and Drug Administration (FDA).
5. Finasteride (Proscar), a 5α reductase inhibitor can lower PSA levels.
6. Digital rectal examination is very useful in primary screening for CA prostate.
7. Men with low initial PSA (< 1ng/mL) can have PSA screening up to once every 4 years.
8. Most authorities worldwide is recommending population screening for men > 50 years old.
9. Men with family history or BRCA1 or BRCA2 mutations carrier may start screening at age 40.
10. Randomised trials show consistent result in reduction of prostate cancer mortality after PSA screening.

ANSWER SHEET FOR SEPTEMBER 2013

Please return the completed answer sheet to the Federation Secretariat on or before 30 September 2013 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

Screening for CA Prostate

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Name (block letters):_____ HKMA No.: _____ CDSHK No.: _____

HKID No.: __ __ - __ __ __ __ X X (X) HKDU No.: _____ HKAM No.: _____

Contact Tel No.:_____

Answers to August 2013 Issue

The Current Status of Minimally Invasive Liver Surgery

1. T **2.** F **3.** F **4.** T **5.** T **6.** F **7.** T **8.** T **9.** T **10.** F

Myths about Food and Cancer: Hope, Hype or Hoax

Dr. Victor HSUE

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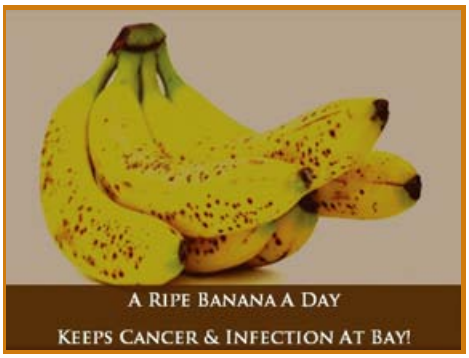
Dr. Victor HSUE

Despite years of research on the effect of food in cancers, there are more and more questions being asked than answered. The vast amount of coverage by the media, including the news, emails, forums and websites can now be conveyed directly to the lay public. Many of these information are not traceable not to mention verified and, even if it is subsequently proven wrong or misleading, it will remain and will propagate in the cyberspace. This makes a layman who would like to seek information in this area extremely difficult to obtain evidence-based information.

A simple search on Google by typing "anticancer food" (searched on August 10, 2013) can link you up to 9,180,000 web pages whereas "cancer causing food" will give you an amazing 174,000,000 web pages. Among these web pages, there are suggestions that common food such as apple and orange can cause cancer. Allegedly apple juice may contain arsenic whereas orange juice may contain excessive antimony. Both agents are possibly carcinogenic when taken excessively.



Even more interesting, a simple search on "banana and cancer" results in 25,100,000 links and while some suggest it causes cancer, some of them suggest banana can even fight cancer, particularly those ripe bananas with dark patches. There are reports suggesting it contains a Tumour Necrosis Factor (TNF), which can fight cancer cells. But in reality eating this TNF, which is protein, is probably of little use, as it cannot go through the digestive system into the circulation.

There are emails in circulation for more than 10 years. One example is about the Johns Hopkins researchers' finding on cold water from plastic bottles in refrigerators is carcinogenic. Johns Hopkins Kimmel Cancer Center has openly stated that this is fabricated news and confirmed that drinking cold water is safe.

Despite the repeated clarifications from the Center, this email hoax never ends and is still circulating in the Internet. Since then the Johns Hopkins Kimmel Cancer Center has set up a web page to denounce these hoaxes. The website is very informative and it can be assessed from this link :

http://www.hopkinsmedicine.org/kimmel_cancer_center/news_events/featured/cancer_update_email_it_is_a_hoax.html.

From this web site, explanations of other common fabricated statements on cancer topics can also be found:

- Everyone Has Cancer Cells
- A Strong Immune System Destroys Cancer
- Cancer is caused by Nutritional Deficiencies and Supplements Will Correct Them
- Chemotherapy and Radiation Therapy Harms Normal Cells. Surgery Causes Cancer to Spread
- Cancers Feed on Certain Foods
- Cancer is a Disease of Mind, Body and Spirit
- Oxygen Kills Cancer Cells

But these false claims have their ways to survive. To increase their credibility, these claims are often linked with important scientific findings, theories or scientists (including Nobel laureates). In fact the false claims have no relevance. Two of the examples are as below:

Warburg effect: This is the observation made by Nobel laureate Otto Heinrich Warburg in that most cancer cells predominantly produce energy by glycolysis followed by lactic acid fermentation in the cytosol. This produces an acidic microenvironment in the tumour. He hypothesises anaerobic respiration in cancer cells occurs even in the presence of oxygen and is the cause of malignancies.

False claims: Tumour cells like acid and will grow faster if the body pH is acidic. Eating an "alkaline diet" can alter the body pH and thence reduce cancer risks.

Fact: All active cells produce acids and an acidic environment of tumours is the result rather than the cause of active cancer growth. Eating alkaline food should have a minimal effect on the body pH due to the acid-base homeostasis through renal and pulmonary functions.

The current knowledge is that mutations in driver oncogenes and tumour suppressor genes are known to be responsible for malignant transformation and this

Warburg effect is considered a result of these mutations rather than the cause.

Folkman's findings on Angiogenesis

In 1971, Dr. Judah Folkman in Harvard Medical School published in the "New England Journal of Medicine" a hypothesis that tumour growth is angiogenesis dependent and that inhibition of angiogenesis could be therapeutic.[9] This article also introduced the term anti-angiogenesis to mean the prevention of new vessel sprout from being recruited by a tumour. He researched on cartilage to search for anti-angiogenic compounds. He reasoned that since all cartilage lacks blood vessels, it must contain some signalling molecules or enzymes that prevent capillaries from forming.

False claims: Sharks do not have cancer and shark cartilage has anti-angiogenesis substances to prevent cancer from growing. A guy called William Lane speculated that oral shark cartilage can prevent or cure cancer and he claimed a Cuban study confirmed the effects. He wrote a best seller called "Sharks Don't Get Cancer" [12] and commercialised shark cartilage.

Fact: The Cuban study had not been published in any peer-reviewed medical journal. The National Cancer Institute (NCI) later concluded that the study results were "incomplete and unimpressive."[12] Shark cartilage was proven to be useless in randomised trials later. The truth is that sharks do have many cancers but of course those are different from human malignancies.

How to know which are hoaxes

Many of this fabricated information are circulated through books, newspapers, magazines, emails, forums and websites. Sometimes it will be very difficult to identify facts from hoaxes. Many of the web or email hoaxes have several distinct characteristics in their content:

1) "Pass this on." "Forward this important information to the people you care about," any email that asks to be forwarded into the inboxes of your friends and family deserves skepticism;

2) Create your emotion, make you feel angry and want to do something about it, e.g. "there is no cancer in human, drug company and healthy authority create it";

3)The original sender is uncertain. The original articles cannot be traced; the author and the scientists cannot be identified;

4) The story or information is difficult to verify. Tales of a conspiracy or cover-up and vague references are used often with technical or scientific-sounding jargon to make it seems plausible and its authors, authoritative.

5) The timing is vague. They refer the time as "last week" or "recently" instead of an exact date. This is to make the misinformation seem important and relevant for an indefinite period of time. In the world of e-rumours, the less specific they are, the longer the lifespan.

6) The viewpoint is one-sided and strong.

7) They often try to create a widespread threat – Health scares often fall into this category. An example is the association of anti-perspirants or cosmetics/shampoo with cancer.

8) When they are questioned about the scientific proof or publication, they will accuse the scientific world of being biased. They claim that their findings when published would affect the funding of the academic research centres and the revenue of the drug industries (as no one will have cancer then!!);

9) Interestingly this kind of emails often says: "This is not a hoax."

There are useful web sites, which help to explain hoaxes and will give a balanced view of these claims:

- http://www.hoaxorfact.com
- http://www.cancer.org/aboutus/howwehelpyou/rumors-myths-and-truths
- http://www.snopes.com

Even with all these resources, it is sometimes difficult for medical professionals to have enough knowledge on every subject. However it will be their responsibility not to play a role to spread rumours without attempting to look for the evidence.

Reports on foods that can cause cancer or prevent cancer are too many to report within the scope of this article. Different countries and cultures all have their folk remedies to prevent cancer. At the same time, there are also suggestions that some foods may cause cancer; these are speculations and nothing more than hearsay. This can cause public concern and fear. If this unfounded fear is excessive the quality of life will be affected.

Below are some common beliefs:

"Foods to prevent cancer ? "

1) Antioxidants

Antioxidants interact with and stabilise free radicals, which may induce cancer formation. Examples of antioxidants include beta-carotene, lycopene (rich in tomato), vitamins C, E, and A, and other substances. There are laboratory evidences from chemical, cell culture, and animal studies indicating that antioxidants may slow down or possibly prevent the development of cancer. However, evidence from clinical trials is not clear.

Five large-scale clinical trials published in the 1990s showed conflicting results about the effects of antioxidants on cancer. The conclusions of each study are summarised in next page (Table 1).

To illustrate the controversy, a recent Physicians' Health Study II involving 14,641 male US Physicians tests the balance of benefits and risks of vitamin E, vitamin C, and a multivitamin. While taking vitamin C and vitamin E supplements did not prevent cancer, daily multivitamin use was associated with a reduction in

total cancers. Among 1312 men with a baseline history of cancer (HR, 0.73; 95% CI, 0.56-0.96; p = .02), but this did not differ significantly from that among 13 329 men initially without cancer (HR, 0.94; 95% CI, 0.87-1.02; p = .15; p for interaction = .07). [9]

Table 1.

Study	Anti-oxidants	Results
Chinese Cancer Prevention Study (1993) [4]	Beta-carotene, vitamin E, and selenium	The combination significantly reduced incidence of both gastric cancer and cancer overall
Alpha-Tocopherol (vitamin E)/ Beta-Carotene Cancer Prevention Study (ATBC) [5] (1994)	Alpha-Tocopherol Beta-carotene	Lung cancer rates of Finnish male smokers increased significantly with beta-carotene and were not affected by vitamin E
Beta-Carotene and Retinol (vitamin A) Efficacy Trial (CARET) [6] (1994)	Beta-carotene and Retinol	Possible increase in lung cancer associated with antioxidants
Physicians' Health Study I (PHS) [7](1996)	Beta-carotene and aspirin	No change in cancer rates associated with taking the combination.
Women's Health Study (WHS) [8] (1999)	Beta-carotene	No benefit or harm from beta-carotene supplementation

There are early results on lycopene suggesting that it may lower PSA in prostate cancer patients but another phase II study suggests lycopene may increase the PSA level on advanced prostate cancers.[12]

The update result of Selenium and Vitamin E Cancer Prevention Trial (SELECT) in 2011 is alarming. This NCI funded trial studies one or both of these substances could prevent prostate cancer when taken as dietary supplements. Since 2001 over 35,000 men, age 50 or older from more than 400 sites in the United States, Puerto Rico, and Canada participated in SELECT.

The initial results published in 2008 found that selenium (0.2 mg) and vitamin E (400 i.u.), taken alone or together did not prevent prostate cancer and the supplement was stopped by the trial. After an additional 18 months of follow up, this update data showed men who took vitamin E alone had a 17 percent relative increase in the number of prostate cancer compared to men on placebo.[16] This difference is statistically significant. Men taking selenium alone, or vitamin E and selenium, were also more likely to develop prostate cancer than men taking placebo, but those increases were smaller and are not statistically significant. The observation that the risk of prostate cancer has continued to increase suggests that vitamin E may have long-term effects on prostate cancer risk.

Therefore based on the current evidence and the controversy in the study results, use of anti-oxidants as dietary supplements to prevent cancer cannot be recommended. However the use of fresh fruits and vegetables as a source of anti-oxidants is always encouraged.

2) Asparagus

There are many claims on the Internet since 2006 about the use of asparagus to cure cancer. This was allegedly based on an article called "Asparagus for Cancer" published in a Cancer News Journal in December 1979. However neither the article nor the journal can be traced and the author "Richard R. Vensal" cannot be identified. There are no published reports on the use of this single vegetable having any effect at all on cancer prevention and cure.

Recently there was a statement broadcast from a commercial radio programme in Hong Kong suggesting that eating a large amount of asparagus everyday can cure cancer. This unfounded statement was broadcasted on radio and subsequently uploaded on the Internet as medical knowledge. It has created interest among lay people and been circulated around by whatsapps and emails in the last few months. This exactly illustrates how rumours can be started and spread.

As Judy Smith, a nutritionist on the Dana-Faber Cancer Centre web page[21] has commented:

Asparagus is a healthy food to include in your diet and does have many benefits, including phytonutrients that can protect against cancer. However, there is no proof that asparagus can cure cancer. Instead of recommending asparagus in particular, we recommend patients follow a plant-based diet rich in fruits, vegetables, and whole grains. Asparagus is a great addition to this type of diet but should not be the main staple of it.

3) Cottage Cheese and Flaxseed oil

In 1950s a German biochemist called Johanna Budwig recommended the so-called "Budwig diet". It involves eating flaxseed mixed with cottage cheese or milk. Budwig believes that the blood of cancer patients is deficient in important nutrients, including phosphatides and lipoproteins. Flaxseed contains high levels of fibre and many vitamins and minerals. The Budwig diet is rich in fruit, vegetables and fibre. Sugar, meat, and fats such as butter, margarine and salad oil are to be avoided.[12]

Apart from the initial claims from Budwig that she had cured many patients, there were only some small laboratories and animal studies on these issues. Even though there is no reliable scientific evidence to show that the Budwig diet has any effect on cancer, commercial products are available.

This diet is not completely safe. There are reports on their side effects including diarrhoea, gas and nausea. There have also been reports of a few allergic reactions. Taking high doses of flaxseed without enough water can cause bowel obstruction.[12]

4) Noni fruits

The noni plant is a tropical evergreen tree that grows in Tahiti and other Pacific Islands, The juice, fruit, bark, and leaves are used in herbal remedies and Polynesian folk medicine. Although animal and laboratory studies have shown some positive effects, there is no reliable clinical evidence that noni juice is effective in preventing or treating cancer. Noni fruit juice and supplements contain various amounts of vitamin C and A, as well as trace minerals.

In 1998 the Attorneys General of Arizona, California, New Jersey, and Texas charged the company that

manufactures noni juice with making unfounded claims on treating cancer. FDA has sent repeated warnings to stop claims that noni could cure, treat, or prevent disease. However, these claims are still widely made on Web sites and elsewhere.[12]

The safety of noni juice also raises concern. In Europe a few cases of liver problems have been reported. One of these patients had previous liver damage and required a liver transplant, but the others recovered when noni was stopped. The abundance of potassium and sugar in the juice is also not suitable for renal or diabetic patients.[12]

5) Organic food

"Organic food" is food that is grown without added synthetic pesticides and fertilisers, growth promoters or genetic modifications. But if the earth is contaminated with chemicals, heavy metals or aflatoxins it can still cause health hazards.

Studies done both in Australia and around the world have not found significant differences in the mineral, trace element or B vitamin content of organic fruit and vegetables and cereals compared to those grown using conventional methods. However some studies suggest that organic foods may be slightly higher in vitamin C.

At present, no research is able to prove if organic foods are more effective in reducing cancer risk than foods produced by other farming methods. Therefore, the choice between "organic" or "non-organic" foods is entirely personal. [14]

"Foods that can cause cancer ? "

1. Sugary Food

It is always advisable for a healthy person to avoid excessive sugary food to prevent obesity and risk of diabetes. However for cancer patients with marginal carbohydrate and protein intake, sugar is an indispensible source of energy. This is even more important for patients on chemotherapy or radiotherapy.

With the increasing use of PET/CT and Standardised Uptake Value (SUV) of the radiolabel (FDG) to reflect the activity or virulence of cancer, sugar uptake in tumours is made visualised. So the rumour says if you eat sugar you are feeding the tumour cells. Of course the rumour makers do not know all carbohydrate, protein and fat can be converted into sugar inside the body.

2. Nutritious food such as Bird's nest

For a layman it is a reflex thinking that having nutritious food can promote the growth of cancer. However for a cancer cell to survive in the host, the cell has adapted itself in the stressed environment and is able to feed on the host. Depriving the host with food will lower the immunity of the host against cancer and also slow down the recovery of the patients from surgery, chemotherapy and radiotherapy.

There are many sayings that bird's nest can promote cell growth and contains hormones, which can increase the chance of cancer recurrence. However a recent literature search on pubmed, medline and medscape does not show scientific reports on this issue. Such a speculation without any evidence base is not limited to bird's nest, it is also extended to fish maw and sea cucumber.

3. "Hormone containing food": Milk, chicken

Recombinant bovine growth hormone (rBGH) is a synthetic hormone to increase milk production in cows. The Food and Drug Administration (FDA) approved it in 1993, but its use is not permitted in the European Union, Canada, and some other countries. The amount of rBGH in milk is reportedly very low and since it is a peptide, ingestion of rBGH is unlikely to produce any effect.[12]

Along the same line the accusation on needled chicken is also unfounded. Chicken is not injected with growth hormone (otherwise they have to be injected thrice per day!) or oestrogen. Flu vaccine is now a routine.

The truth is that no hormone has been allowed in poultry production for more than 50 years as hormone use in poultry production was banned in the United States in the 1950s.[11]

4. Certain meat: beef, shelled fish, eel etc

There is misunderstanding that beef is the only common red meat. In fact lamb, pork (even it turns white after cooked), duck, goose and chicken leg are considered red meat. There is a general recommendation to limit the amount of red meat per day. But a moderate amount of red meat has no association with increased cancer risk.

Eating shelled fish or eel may cause allergy in certain individuals and if eaten raw may cause diarrhoea but there are no data to suggest it has any association with increased cancer risk.

5. All preserved food or fermented food

It is always true to prefer fresh food including fruits and vegetables rather than preserved food. But occasional consumption of well-preserved food like ham and sausage or prickle is unlikely to do harm.

Bread, cheese, vinegar, and soybeans are all made by fermentation. The only well known fermented food to cause cancer is alcohol. To generalise all fermented food can cause cancer is certainly a rumour.

6. Soy

There are more controversies in soy than in other foods. In a 1981 prospective study in Japan, researchers found that daily intake of miso was linked to lower death rates from stomach cancer in more than 260,000 men and women. East Asians with high soy consumption have a lower incidence of hormonal responsive tumours like carcinoma of breast and prostate.[12]

Soy contains Isoflavones, which may act like oestrogen (phytoestrogens). They also have anti-oestrogen properties. Isoflavones include Genistein, daidzein, and glycitein.

A number of laboratory and animal experiments and human observational studies suggest that soy may reduce the risk of several types of cancer, including breast, prostate, ovarian, and uterine cancer.

A meta-analysis of 18 epidemiologic studies (12 case–control and six cohort) shows a small reduction of breast

cancer risk by soy intake, however, this result should be interpreted with caution due to potential exposure misclassification, confounding, and lack of a dose response, recommendations for high-dose isoflavone supplementation to prevent breast cancer or prevent its recurrence are premature.[17]

On the other hand there are also cell lines and animal experiments with mice injected with ER-positive tumour cells when varying doses of genestein or daidzen. Those given more of the isoflavones had a greater growth of the breast tumours compared to mice given little or no isoflavones.[18] This and similar studies have created fear among women particularly those vegetarians who rely on soy as the main source of protein. However even children know humans and mice are different.

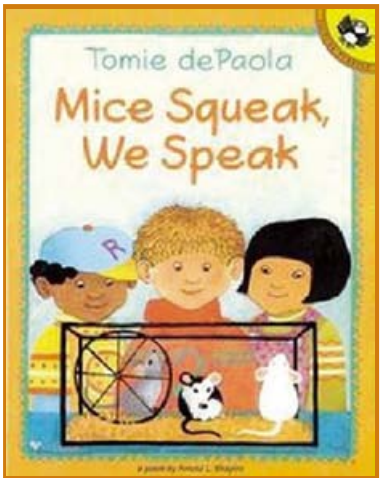


Figure 2: Front cover of a children's book by Tomie dePaola

Human studies are important. Several studies of men with prostate cancer have suggested that soy foods and/or supplements may reduce levels of prostate-specific antigen.[12] A randomised trial[19] was done to see the effect of oral intake of soy protein isolate for 2 years on a group of carcinoma of prostate patients after radical prostatectomy. The result showed that the supplement did not reduce or delay development of biochemical recurrence of prostate cancer compared to men who had received placebo. Thus the authors concluded:

"The findings of this study provide another example that associations in observational epidemiologic studies between purported preventive agents and clinical outcomes ***need confirmation in randomised clinical trials****. Not only were these findings at variance with the epidemiologic evidence on soy consumption and prostate cancer risk, they were also not consistent with results from experiments with animal models of prostate carcinogenesis, which also suggest reduced risk,"* [19]

Despite the lack of proven benefit of isoflavones supplement in preventing cancer, a moderate daily consumption of soy products has never been shown to be associated with increased cancer risk in human studies and is considered safe.

Others

There are many other foods that are suggested to have anti-cancer properties, this will include various types of mushrooms: Linzhi (Ganoderma lucidum) 靈芝 , Yunzhi (Coriolus versicolor) 雲芝 , Shiitake Mushroom (Lentinus edodes) 椎茸 , Maitake (Grifola frondosa) 舞茸 and Agaricus Blazei Mushroom 巴西蘑菇 (姬菇茸). There are laboratories and animal studies suggesting they may be of some use. Clinical studies are mainly performed in China and Japan. Human studies results are controversial and large well-controlled randomised trials are still awaited.

Recommendations

The American Cancer Society's most recent nutrition guidelines[13] recommend eating a balanced diet with an emphasis on plant sources, which includes:

- 5 or more servings of vegetables and fruits each day
- Choosing whole grains over processed and refined grains
- Limiting processed meats and red meats
- Balancing calorie intake with physical activity to get to or stay at a healthy weight
- Limiting alcohol intake

An authoritative source of information on diet, physical activity and cancer is the book "Food, Nutrition, Physical Activity, and the Prevention of Cancer: A Global Perspective", published by World Cancer Research Fund in 2007. This second report both in English and Chinese can be downloaded.[15]

Their recommendations for cancer prevention and good health are:

- Be as lean as possible without becoming underweight.
- Be physically active for at least 30 minutes every day.
- Avoid sugary drinks. Limit consumption of energy-dense foods (particularly processed foods high in added sugar, or low in fibre, or high in fat).
- Eat more of a variety of vegetables, fruits, whole grains and legumes such as beans.
- Limit consumption of red meats (such as beef, pork and lamb) and avoid processed meats.
- If consumed at all, limit alcoholic drinks to 2 for men and 1 for women a day.
- Limit consumption of salty foods and foods processed with salt (sodium).
- Don't use supplements to protect against cancer.

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Where Are We in the Treatment of Advanced Colorectal Cancers?

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Introduction

Colorectal cancer is the second most common cancer in Hong Kong edged marginally by lung cancer in 2010[1]. It represents over 1800 and is also the second leading cause of cancer-related deaths.

Patients who are diagnosed with invasive colorectal cancer suitable for resection require a complete staging work up. This comprises of pathological confirmation, total colonoscopy, complete blood counts, chemistry profile, carcinoembryonic antigen (CEA), baseline CT scans and sometimes PET/CT as needed.

Challenges of Treatment

Some unfortunate patients present with overt bowel obstruction. This would mean resection with diversion, stent insertion and temporary diversion are the only practical options. Stent insertion followed by systemic combination treatment has grown in popularity in recent years turning the bulky tumour and the patient into a more favourable state for resection.

Even for those patients who have received clear operations up front, the risk of microscopic residual disease is considerable. In general, stage III tumours have a 60% risk of disease recurrence[2], whereas stage II and I tumours have a lower risk of recurrence of 20% and 10% respectively.

For metastatic disease, it usually spreads to the liver, lungs, and peritoneum while bones, ovaries and the brain are less commonly involved. Traditionally, the systemic dissemination of cancer rendered these patients beyond cure.

Ways to improve treatment outcome

Adjuvant chemotherapy is recommended for patients with stage III and poor risk stage II disease[3]. The risk factors include T4 tumours (stage IIB/IIC), poorly differentiated histology, lymphovascular invasion, bowel obstruction/perforation, close resection margins or less than 12 sampled lymph nodes. No adjuvant chemotherapy is recommended for patients with stage I disease.

Recent development of better chemotherapeutic agents, target therapy and an increasingly aggressive surgical approach with caution to metastasectomy has led to a paradigm shift. To date, a growing number of these patients are now assessed with the possibility of cure in mind. This applies specifically to patients with limited metastases to the liver or lung, where survival rates of 5 years following resection in recent reports surpass 40% and 50% respectively.

Development of chemotherapy

Use of adjuvant fluoropyrimidine-based chemotherapy developed in the 1970's is well established, resulting in approximately a 25% reduction in the risk of death. This is equivalent to an absolute benefit in 5-year overall survival of 4–12%. The optimal 5-fluorouracil (5-FU) regimen has evolved over the past 30 years. Bolus 5-FU given at a dose of 370–500 mg/m2 is the basis of most adjuvant regimens. A total of 6 months of 5-FU modulated by low-dose folinic acid appear to be an optimal regimen in the last decade. Infusional 5-FU schedules have been shown to have better clinical outcomes despite the inconvenience in delivery. Recent evidence also suggests that oral fluoropyrimidines such as oral capecitabine (Xeloda) and tegafur (UFT) are as effective as infusional 5-FU schedules. Actually, oncologists are now more concerned about the problem of oral drug compliance than the efficacy.

The European MOSAIC trial with a median follow up of 6 years confirmed clear improvement in disease free survival DFS and overall survival in using FOLFOX (infusional 5FU + Oxaliplatin) compared with infusional 5FU[4]. XELOX (Xeloda + Oxaliplatin) was shown to have similar efficacy to FOLFOX in the AVANT trial. The current standards for treating stage III disease after primary surgical treatment are FOLFOX and XELOX. Despite intensive research, there is no established benefit in the use of bevacizumab, cetuximab, panitumumab or irinotecan under adjuvant settings.

Why rectal cancers differ from colon cancers?

The location of any malignant tumour below the level of the peritoneum reflection in the pelvis differentiates rectal from colon cancers. The origins of the gut cells are similar and yet the lack of peritoneal blanket, close proximity to other pelvic structures and technical difficulties in obtaining wide margins especially in the male pelvis renders advanced rectal cancers to have a higher propensity of local relapse.

Total mesorectal excision (TME) is recommended for advanced rectal cancers. The surgery includes an en

bloc removal of mesorectum, including vascular and lymphatic structures, fatty tissues and mesorectal fascia through sharp resection while sparing the autonomic nerves. Sphincter preservation is preferable but not possible in all patients.

Adjuvant radiotherapy may have a role in the loco-regional control of locally advanced colon cancers, particularly for tumours involving the posterior wall of the retroperitoneal portion of the colon, but this is controversial. Reduced loco-regional recurrences and improved survival in patients treated with radiotherapy following complete resection of the colon cancers have been reported in small case series, primarily in patients with T4 disease or positive lymph nodes. At present, radiotherapy is not part of the routine treatment of colon cancers. On the other hand, use of radiation in rectal cancers is supported by strong evidence.

Adjuvant treatments before the wolves come

In contrast to adjuvant treatment of colon cancers focusing on preventing distant metastasis, comprehensive rectal cancer treatment often includes loco-regional treatment due to a relative high recurrence risk.

Several multicentre trials of either pre- or post-operative radiotherapy in resectable rectal cancers have demonstrated reduced local recurrence rates compared with surgery alone. This difference is present even after the optimisation of rectal surgery, as demonstrated in the Dutch TME trial in which all patients underwent rectal resection with TME. In this study, the relative reduction in local failure with addition of radiotherapy was in fact even greater than seen in studies utilising standard rectal cancer surgery.

For the majority of locally advanced (stage II/III) rectal cancer patients, adjuvant treatment with surgery, radiation therapy and chemotherapy are recommended. The problem is whether chemotherapy and radiotherapy should be given before or after the definitive surgery.

Neo-adjuvant Vs Adjuvant treatment

Neo-adjuvant radiotherapy (before surgery) is more preferable than given postoperatively[5,6]. Firstly, the local recurrence risk reduction appears to be greater with pre-operative treatment. Secondly, the efficiency of radiation per dose is higher in the pre-operative setting because of better oxygen delivery to tissues before surgical dissection. Thirdly, pre-operative radiation offers a slight improvement in overall survival which is not seen with post-operative radiation. Fourthly, post-operative radiotherapy results in higher toxicity than pre-operative treatment. This is related to the use of relative higher doses and the exposure of more residual tissue to radiation when given postoperatively. Lastly but surely not the least, trials of pre-operative rectal irradiation have shown significant down-staging of tumours at all stages. This means less extensive resection, higher chances of sphincter preservation and more resectable tumours.

Combining chemotherapy with radiation confers an even greater advantage than achieved by either modality alone[7]. A review of all randomised trials comparing pre-operative radiotherapy to pre-operative chemo-radiotherapy in stage II and III rectal cancers found a significant decrease in local recurrence and a significant increase in pathological complete response with chemo-radiotherapy, although there was no significant difference in rates of sphincter preservation or overall survival at 5 years. The rates of post-operative morbidity, including anastomotic leaks, were the same in both groups.

On the other side of the coin, the major drawback of neo-adjuvant therapy is the possibility to over-treat some patients. Rectal cancer staging using endorectal ultrasound or MRI retains some degree of inaccuracy, and a certain proportion of patients with pre-operatively staged T3 tumours or node-positive disease will ultimately be found to have stage I disease. Such patients may be unnecessarily exposed to the toxic effects of chemo-radiation without any added benefit. However, with further technical advances in staging work up and balancing all the parameters, preoperative concomitant chemotherapy and radiotherapy is regarded as the standard nowadays.

To catch the get away

With the unique venous drainage by the portal system, liver metastases are the most common metastatic site in colorectal cancers. They are present in 15–25% of patients when diagnosed with the primary tumour and will develop in another 40–50% of patients following treatment of the colorectal primary.

The 5-year survival rate for patients undergoing a curative liver resection is about 40%. The mean survival for untreated metastases is 6–12 months, which can be extended to 12–18 months with the newer chemotherapy regimens. The majority of patients diagnosed with metastatic colorectal cancer have unresectable disease. However, the cohort with liver-limited disease might be converted into resectable disease with the advent of systemic chemotherapy and target therapy. It has to be noted that irinotecan and oxaliplatin-based chemotherapy may cause liver steatohepatitis and sinusoidal liver injury. It would be advisable to perform surgery once the patient is considered resectable avoiding overcooking the condition with excessive treatment cycles. Two factors clearly associated with poorer outcome are positive resection margins and the presence of extrahepatic disease at the time of liver resection.

The coming sunshine

In terms of recent breakthroughs in colorectal cancer treatment in the last decade, the most prominent of these has been the introduction of target therapy. They are antibodies directed against the epidermal growth factor receptor (EGFR) as well as antiangiogenic antibodies directed against the vascular endothelial growth factor (VEGF).

In the first category, the chimeric antibody cetuximab[8] and the humanised antibody panitumumab are among the most extensively studied for CRC., They function by binding to the extracellular domain of EGFR, inhibiting

its function in tumour proliferation and metastasis. Research work has shown tumours with mutations in exon 2 of the KRAS gene are insensitive to either of them. Recent development suggests confirming all the KRAS and NRAS genes in exon 2, 3 and 4 altogether. In other words, genotyping of the tumour tissue confirming no mutation or wild type of all RAS genes is needed to select patients who might benefit from the treatment.

Bevacizumab is an antibody targeted against VEGF which acts by inhibiting the proliferation of new blood vessels to the tumour. The addition of bevacizumab to first line chemotherapy in metastatic disease can have modest clinical benefits[9]. Use of bevacizumab interferes with wound healing and is not advisable for use less than 6 weeks post operation. The risk of strokes and other arterial events are increased among bevacizumab users especially in those above 65 years. The rare side effects of gastrointestinal haemorrhage and perforation is also noteworthy. However, worries about the rebound of disease after cessation of bevacizumab lack clinical evidence to support it. Singleton usage of bevacizumab is not recommended as it has inferior efficacy compared with FOLFOX alone or FOLFOX plus bevacizumab.

Aflibercept functions as a VEGF trap to avoid activation of the VEGF receptors and inhibits angiogenesis. The drug works on a similar target as bevacizumab and is used as a second line treatment option in combined use with FOLFIRI (5FU + Irinotecan)[10]. The common side effects include fatigue, infection, diarrhoea, hypertension and venous thromboembolic events.

Regorafenib is the first oral multiple kinases inhibitor therapy for patients refractory to chemotherapy irrespective of KRAS status[11]. The hand-foot skin reaction, fatigue, hypertension and diarrhoea are the common side effects.

All target drugs are by far not harmless, just having different side effects in normal tissues. Yet in general, the extent and severity would be much less than using chemotherapy alone.

Longing for a better future

With multidisciplinary management of patients with liver-limited metastatic colorectal cancer, cure of certain patients can be a realistic goal. The standard curative treatment of patients with colorectal cancers is liver resection or local ablative treatment using radio frequency. These approaches result in a 5-year survival rate of 25–58%[12]. In addition, the use of new drug combinations such as 5-FU/folinic acid with oxaliplatin[13] or irinotecan has increased the overall survival rate. More importantly, these drug combinations have down-sized tumours to enable resection with organ preservation and increase the 5-year survival rate. The success of this multi-drug chemotherapeutic approach is still further enhanced when appropriate target agents are added.

Remarkable forward strides were made in terms of patient lives saved and quality of life gained in the past decade. The optimal approach is in continuous evolution with more weapons equipped by us. The future direction would be more personalised treatment with tailored local and systemic treatment for patients yielding best clinical outcome.

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Some Interesting Issues in Early Colorectal Cancer

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Colorectal cancer (CRC) is special not just because of its high prevalence in an affluent society like Hong Kong. Its strong link to inheritance and environmental factors is striking. It is also one of the very few deadly cancers that population screening might have significant impact to patient survival.

CRC is the second most common cancer in Hong Kong with 4,370 new cases in both sexes in the year 2010. Median age of diagnosis is 70. Male to female ratio is 1.3 to 1. The lifetime risk for colorectal cancer is estimated to be 1 in 22 among males and 1 in 34 among females[1].

In the United States, the overall incidence of colon cancer has diminished slightly by 2.2% in women and 2.8% in men in the past three decades[2].

Both environmental and genetic factors can increase the likelihood of developing CRC. Although inherited susceptibility results in utmost increases in cancer risk, most CRCs are sporadic rather than familial.

Genetic Predisposition

Despite less than 10% of colon cancers are associated with a true inherited polyposis-related condition, a family history of CRC in a first-degree relatives is an important risk factor and accounts for up to 20% of all affected patients. The relative risk (RR) associated with a single first degree relative with adenomas is 1.74 (95% CI 1.24–2.45) over the general population[3].

Management of inherited syndromes should not just focus on the affected individual. The importance of identification and surveillance of unaffected family members is never overemphasised.

The Lynch Syndrome or hereditary non-polyposis colorectal cancer (HNPCC) is an autosomal dominant syndrome caused by a germline mutation in one of the genes involved in DNA mismatch repair and accounts for up to 3-5% of all CRCs. The adenomas are usually less than 10 in number and invasive tumours are more on the right side. The cancer risk by age of 60 is 50 to 80%. It is molecularly characterised by microsatellite instability and clinically characterised by early-onset proximal colon cancers. It can also manifest itself as endometrial cancer, cancer of the ureter and renal pelvis, small bowel, gastric, ovarian, pancreatic and biliary cancers[4].

Familial adenomatous polyposis (FAP) is also an autosomal dominant syndrome caused by a germline mutation in the adenomatous polyposis coli (APC) gene and accounts for less than 1% of all CRCs. It is characterised by literally thousands of early-onset colorectal polyps with 100% penetrance for colorectal cancer. FAP carries an increased risk of adenocarcinomas of the duodenum, jejunum, pancreas and biliary tree in addition to thyroid cancers and gliomas.

Some guidelines recommend APC genetic testing for FAP in all patients with clinical evidence of greater than 100 colorectal adenomas, and for all first-degree relatives of FAP patients[5]. Prophylactic total colectomy is the ultimate surgical management of FAP.

A rare autosomal dominant disorder, Peutz-Jeghers syndrome, is a associated with an increased risk of multiple cancers including the colorectum.

It is believed that patients who have a family member with an adenomatous colonic polyp may also be at increased risk for adenoma or colorectal cancer. Some guidelines recommend early screening (age 40 years) for people with a family history of polyps in relatives <60 years old[6].

Inflammatory Bowel Disease

Ulcerative colitis is strongly linked with CRC. Some retrospective analyses suggested that widespread colitis causes a 15-fold increase in cancer risk beginning about 8 years after initial diagnosis[7]. This risk is further increased in the presence of primary sclerosing cholangitis and pseudopolyps. Although there are much less data, it appears that pancolitis due to Crohn's disease is associated with a similar relative risk of colon malignancy as extensive ulcerative colitis. Annual surveillance colonoscopy with random biopsies has been recommended after 8 years of colitis, with colectomy recommended in the presence of high grade dysplasia[8].

Personal or family history of sporadic CRCs or adenomatous polyps

Patients with a personal history of CRC or adenomatous polyps of the colon are at risk to future development of colon cancers. In patients undergoing resection of a single CRC, metachronous primary cancers develop in 1.5 to 3 percent of patients in the first five years postoperatively. A personal history of large (>1 cm) adenomatous polyps and polyps with villous or tubulovillous histology also increase the risk of CRC, particularly if multiple[9]. The relative risk ranges from

approximately 3.5 to 6.5 in such patients. On the other hand, as a group, patients with one or two small (<1 cm) tubular adenomas do not appear to be at substantially increased risk of metachronous CRC.

A family history is also an important risk factor even outside of the syndromes with a defined genetic predisposition. Having a single affected first-degree relative with colorectal cancer increases the risk about twofold over that of the general population. The risk is further increased if two first-degree relatives have colon cancer or if the index case is diagnosed below 50 to 60 years of age.

Environmental factors

The association between a Western diet that is low in fruits and vegetables and high in red meat and animal fat has been the subject of numerous cohort studies. In a pooled analysis including over 14 studies with more than 750,000 participants, fruit and vegetable intake was associated with a 26% relative reduction in risk of distal colon cancers, but not with overall colon cancer risk[10]. Similarly, a high intake of red and processed meat has been associated with an increased risk of distal colon cancers[11].

Dietary fibre has been postulated to be protective by absorbing faecal carcinogens, altering bile acid metabolism and reducing colonic transit time. Despite cohort studies supporting an association, a systematic review of five randomised trials evaluating dietary fibre in the prevention of colorectal cancers demonstrated no evidence of reduced risk of colorectal adenomas with increased fibre intake[12].

The benefits of physical activity and reduced risk of colon cancer gathered a relatively sound epidemiological correlation. Lack of physical activity, central adiposity and a high body mass index are all believed to enhance the mitogenic potential of hyperinsulinaemia. Insulin-like growth factors have also been linked to cellular proliferative and anti-apoptotic effects. In a meta-analysis of 52 studies examining physical activity in primary prevention of colorectal cancers, there was a 24% RR reduction of colon cancer when comparing the most against the least active individuals across all studies (RR 0.76, 95% CI 0.72–0.81)[13].

Abdominal radiation

Adult survivors of childhood malignancy who have received abdominal radiation are at significantly-increased risk of subsequent gastrointestinal neoplasms, the majority being colorectal cancer. Guidelines from the Children's Oncology Group recommend colonoscopy every five years for survivors of childhood cancer who have received 30 Gy or more of abdominal radiation, with screening beginning 10 years after radiation or at age 35 years, whichever is later.

CRC Screening

CRC is essentially a preventable disease. It has a long latency period, and it takes several years for a precursor polyp to transform into a malignant growth. These characteristics render CRC an attractive target for screening. Colon cancer mortality is mostly influenced by the stage of the disease at diagnosis. 5-year mortality in stage I disease is less than 10% but stage IV colon cancer has over 90% 5-year mortality. Identifying colon cancers prior to the development of symptoms is critical in reducing mortality.

Analysis based on pooled data from the Surveillance Epidemiology and End Results (SEER) programme and the CDC's National Programme of Cancer Registries found that over the past 20 years, the CRC incidence declined by 22% while CRC mortality declined by 26%.

A family history is an important risk factor and most guidelines recommend a more aggressive approach in these patients. The guidelines are most uniform when the affected relative developed neoplasia at younger age (e.g., <60). Starting earlier and using colonoscopy as the modality for screening are well justified.

Currently, there are indirect and direct methods of screening for colon cancers and precursor lesions. Indirect methods include faecal occult blood testing (FOBT) and faecal immunochemistry tests (FIT). Flexible sigmoidoscopy (FS), colonoscopy, double contrast barium enema (DCBE) and computed tomography colonography (CTC) are direct methods.

Risk Category	Recommended	Interval
Average Risk		
	FOBT	Annual
	FIT	Annual
	Flexible sigmoidoscopy to 40cm	Every 5 yr
	DCBE	Every 5 yr
	CT colonoscopy	Every 5 yr
	Colonoscopy	Every 10 yr

Current screening guidelines are not stratified by sex or by age between the onset of screening (50 years old in average risk individuals) and the age at stopping (70 to 80 years old), even though an individual's risk of colorectal cancer rises rapidly during that time. For a family history of colorectal cancer or adenomatous polyps, screen at 40 years old or 10 years younger than the youngest relative with colorectal cancer is recommended.

Colonoscopy involves direct endoscopic visual evaluation of the entire colon. It allows evaluation, prevention with endoscopic polypectomy and diagnosis with biopsy for CRC. A complete bowel cleansing is advisable the night prior to the test and sedation is needed.

Interestingly, colonoscopy is more effective in preventing left sided than right sided CRCs. Poor right-sided bowel preps, incomplete colonoscopy and anatomical configurations compromising visibility can all be related. However, tumour biology may also have a role between the right and left colon. Serrated adenomas, which are flatter and more difficult to visualise endoscopically are more common in the right colon.

Malignant Polyps

Adenomatous polyps occur in close to 20% of adults

over the age of 60 years old who live in the Western countries. Most of these premalignant adenomatous polyps are amenable to endoscopic removal for definitive treatment. Colonoscopic removal of these polyps has been shown to reduce the risk of colon cancer. However, up to 5% of polyps that appear grossly benign will contain invasive cancer.

It is important to distinguish a malignant polyp from a polyp with carcinoma in-situ or high grade dysplasia. These entities have no appreciable metastatic potential and are cured by polypectomy if the pathologic assessment is adequate and the specimen can be removed in total.

A malignant polyp consists of adenocarcinomatous cells that invade into the submucosal layer of the bowel wall. Pathologically, a malignant polyp is a T1 colon cancer which carries substantial risks of mesenteric lymph node spread rendering segmental resection is a logical treatment choice.

After studying the relation of lymph node positivity with constellation of tumour factors, the American College of Gastroenterology guidelines[14] recommend that malignant polyps be treated with endoscopic removal and close surveillance when the polyp is completely excised.

- the polyp can be accurately assessed with respect to the depth of invasion, grade of differentiation and completeness of excision of the carcinoma.
- the cancer is not poorly differentiated.
- there is no vascular or lymphatic involvement.
- the margin of excision is not involved.

Surgical Management of the Primary Tumour

Surgery is the mainstay of treatment in early stage CRCs. Despite advances in adjuvant therapy, surgical removal of the primary cancer and all macroscopic disease is necessary to achieve cure. Entire lymph node basin removal is also part of the curative procedure allowing proper staging of the disease. Patients with associated conditions (e.g., ulcerative colitis, Crohn's colitis, FAP, HNPCC) will have more extensive surgery to remove the expected risks. The risk of metachronous cancer would balance against the possible functional consequences of extensive colectomy.

Johnson et al. used the Surveillance, Epidemiology and End Results (SEER) data to analyse the impact of the number of disease-free lymph nodes harvested on survival in patients with stage III colon cancers[15]. In 20,702 patients with stage III disease, patients with >13 negative lymph nodes had better survival than patients with fewer than three negative lymph nodes. Furthermore, in patients with stage IIIB and IIIC colon cancer, there was a statistically significant reduction in survival with fewer lymph nodes retrieved.

Although operating times are longer with the laparoscopic approach, hospital stay and postoperative pain are consistently better with minimally invasive surgery[16]. A recent Cochrane review evaluated 12 trials in which 3,346 patients were randomised to either open or laparoscopic surgery[17]. At minimum 2-year follow-up, there was no differences in cancer related mortality.

Adjuvant Chemotherapy for stage II tumour

There are lots of debates on this hot topic. The ASCO expert panel suggested that adjuvant therapy of stage II colon cancer be considered for patients with high risk factors including those patients with inadequately sampled nodes (<13), T4 primary lesions, perforation, obstruction, lymphovascular invasion or poorly differentiated tumours. Anyway, It should not be administered as a matter of routine.

Additional molecular markers of interest have since emerged to select suitable patients for adjuvant therapy in stage II disease. MSI-H tumours are associated with a more favourable prognosis. In addition, MSI-H tumours may be less responsive to 5-FU chemotherapy[18]. A retrospective pooled correlative analysis revealed that patients with MSI-H tumours (deficient MMR) treated with 5-FU had a 5-year DFS which was similar to patients treated with surgery alone (70 vs. 67%, p = 0.30).[19]

In addition to conventional pathologic features and MSI status, development and validation of different gene signature models to predict recurrence risk in stage II colon cancer are under active research.

Summary

Apart from the decrease in CRC incidence, the 5-year survival rates of CRC have improved from 52% in 1975 to 65% in 2004[2] in the United States. In recent years, better public awareness of the disease and higher penetration of screening procedures are noted in this locality. Together with further improvement in therapeutic armamentarium, it would be expected that Hong Kong would follow this trend in the coming years or decades.

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Highlights in Nasopharyngeal Carcinoma

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Nasopharyngeal Carcinoma (NPC) is one of the commonest cancers in Hong Kong, according to the Hong Kong Cancer Registry's 2010 data, it has an annual age standardised incidence rate of 13.9 for males and 4.0 for females, and ranks sixth in males and thirteenth in females among the various cancers in the city. The median age at diagnosis in 2010 is 52, though in the past years this has been in the mid-forties. The male:female ratio is 3:1.[1] This article serves to highlight some of the aspects which are important to general practitioners or family physicians in diagnosis, follow up, and general counselling and support of their patients.

Presentation

Professor John H.C. Ho has described the 5 cardinal symptoms of NPC as follows[2]:

1. Nasal: blood-stained post-nasal discharge, epistaxis, nasal blockage
2. Aural: tinnitus, ear blockage, impaired hearing
3. Headache
4. Cervical lymphadenopathy
5. Cranial nerve palsies: diplopia, dysarthria, sensory loss over the face

Groups 1 to 2 occur in relatively early stages, while groups 3-5 signify more locoregionally advanced disease with the tumour eroding the base of the skull or with already clinically detectable lymphatic spread. Patients may present with only one group of symptoms, or several simultaneously. Persistent nasal or aural symptoms, or cervical lymph node enlargement should prompt the family physician to refer the patient to an otorhinolaryngologist for proper examination of the nasopharynx. Persistent and severe headache often leads to the diagnosis when a MRI scan of the brain is done to elucidate the symptom, whereupon erosion of the base of the skull by a nasopharyngeal mass is demonstrated. Patients with cranial nerve palsies are not infrequently first referred or presented to ophthalmologists or neurologists/ neurosurgeons, and often on undergoing MRI brain is the underlying pathology revealed.

Diagnosis

Faced with suspicious symptoms, the family physician may check the first line investigations which include serological test and image study, while referral to an otorhinolaryngologist for nasopharyngeal examination and biopsy will establish the final diagnosis.

Concerning the serological test, the EBVDNA test has replaced the IgA antibody against EBV as the preferred test. The quantitative PCR test of EBVDNA has a sensitivity and specificity of over 90%. More importantly, it can serve as a monitor of treatment response as well as possibly an initial prognostic marker.[3,4,5] The old time IgA antibody, although helpful in the initial diagnosis, remains positive even after cure of the cancer, and thus checking it after treatment should be discouraged as this often generates unnecessary anxiety in patients who are cured but still have a positive antibody titre. Of great importance is the need to point out that a negative EBVDNA or IgA result does not exclude the diagnosis of NPC. There are many patients with histologically confirmed NPC whose serological test result is negative. Nasopharyngeal biopsy is mandatory if clinically there is a high suspicion of NPC despite a negative serology test.

As for the imaging, MRI of the nasopharynx is the preferred first image study. This shows the soft tissue involvement more clearly than CT scans. In addition, since all patients will have a contrast CT scan done in a mould or cast for modern day radiotherapy planning technique, there is no need to order this prior to radiotherapy planning.

Staging

Fig 1 shows the simplified version of the current AJCC/ UICC staging system[6]. The staging method actually starts with a clinical examination as cranial palsy is elicited at the bedside. Endoscopy is part of the staging procedure as it can show subtle mucosal involvement especially of the choanae and posterior part of the nasal cavities/nasal septum which may not even be apparent on cross sectional MRI. This subtle mucosal spread is important to detect as it is mandatory to accurately include such in the high dose zone of the radiotherapy plan. Locoregional disease is delineated by a combination of MRI and CT scan findings, while distant metastasis work up requires the minimum of CXR and U/S of liver. While for early stage NPCs after the above tests when staging is considered complete, for more locoregionally advanced disease such as those with a bulky primary, evidence of skull base invasion, and significant cervical lymphadenopathy, a PETCT scan is recommended as this would demonstrate the presence of mediastinal lymphadenopathy, small volume lung / liver metastases, and bone metastases which would not be apparent from the basic investigations.

Primary tumour (T)	
T1	Tumour confined to nasopharynx, +/- nasal cavity or oropharyngeal extension*
T2	Tumour with parapharyngeal extension
T3	Tumour involved bones of skull base +/- paranasal sinuses
T4	Tumour with involvement of cranial nerve, orbit, hypopharynx, intracranial content, or infratemporal fossa
*(nasal cavity/oropharyngeal extension are still regarded as T2 by some centres)	
Regional Lymph Nodes (N)	
N0	No regional lymph node metastasis
N1	Metastasis in retropharyngeal node, or unilateral cervical node < 6 cm above supraclavicular fossa
N2	Metastases in bilateral cervical nodes < 6 cm above supraclavicular fossa
N3	Metastases in a node > 6 cm, or to supraclavicular fossa
Distant Metastasis (M)	
M0	No distant metastasis
M1	Distant metastasis
Stage Grouping	
Stage I	T1N0
Stage II	T2, or N1 reached
Stage III	T3, or N2 reached
Stage IVA	T4 reached
Stage IVB	any N3
Stage IVC	any M1

Fig 1. Simplified version of AJCC/UICC staging of NPC 2010

Treatment

For stage I-IVB, the patients are potentially curable. Treatment must be of radical and curative intent. Radiotherapy is used alone for stage I disease, and in combination with chemotherapy for stage II-IVB disease. Stage IVC patients are not hopeless. Even for those with isolated or low volume metastatic disease confined to the mediastinal lymph nodes, or an isolated secondary in the lung or liver, occasional incidents of long term cure have been achieved. Although patients presenting with multiple and extensive distant metastases are not curable, significant prolongation of survival with good quality of life can be achieved with palliative chemotherapy.

Radiotherapy

Radiotherapy (RT) is the cornerstone of curative treatment for NPC. The use of 2D, or 3D conformal technique, and brachytherapy / stereotactic radiotherapy (SRT) boost in various combinations has achieved a high local control rate for the primary tumour in the nasopharynx and metastatic cervical lymph nodes in the past. In recent years, the standard of cure has moved to using the intensity modulated radiotherapy (IMRT) technique, whereby the tumour target volume is irradiated by using multiple beamlets delivered through multiple fields distributed in 360 degrees around the patient. This results in a concentrated high dose region that conforms to the shape and volume of the tumour target region, while minimising the dose to the surrounding normal structures which have radiation dose tolerance limit below the tumoricidal level. The net result is an increase in the therapeutic ratio with an increase in dose delivered to the tumour and a decrease in dose to the critical structures.[7,8,9] Thus there is reduction of the acute side effects such as mucositis, as well as the late side effects such as xerostomia, deafness, cranial nerve palsies and temporal lobe necrosis. Fig 2 shows the radiation dose distribution using IMRT for a typical NPC patient. The total dose is usually given over 33-36 daily fractions, with the treatment period lasting from 6 to 7 weeks. The accuracy of daily treatment set up can be further enhanced with the use of Image Guided Radiotherapy (IGRT) whereby at each treatment fraction, a KV or MV CT scan of the patient immobilised in the treatment position is done with the treatment machine, and any discrepancy in positioning is first corrected by fusion of the immediate CT scan with the planning CT scan before the actual treatment begins.

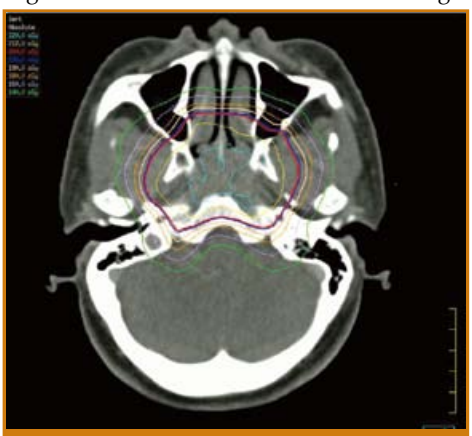

Fig 2. Typical dose distribution in IMRT for NPC. Coloured lines represent isodose lines. The high dose volume conforms to the tumour volume with rapid dose fall off in adjacent structures

Chemotherapy

The main cause of death in NPC is from distant metastases nowadays. Hence intense research is being done on the role of systemic chemotherapy (CT) in combination with radiotherapy for stage II – IVB patients. Such a combination can be in the form of giving CT pre-RT (induction or neoadjuvant), concurrent with RT, or post-RT (adjuvant). The overall conclusion from various randomised trials and meta-analysis is that chemotherapy does improve overall survival by about 6-10%[10,11,12,13], but that the most important contribution of CT is when it is given concurrently with RT. However, when only concurrent CT is given, the chance of eradicating distant metastases is hampered by the necessary reduction in the dose and duration of CT because the acute toxicities of concurrent CT-RT limit the dose, and the duration of CT is only about 6-7 weeks. To further enhance the curative effect of systemic CT, attention must be given to adjuvant or neoadjuvant full dose CT in addition to the concurrent phase of CT-RT.

The value of post-RT adjuvant CT is still debatable. The trial by Al-Sarraf reported in 1998[14] in which CT with cisplatin q 3 week x 3 is given concurrently with RT, followed by 3 more cycles of cisplatin/5FU showed an improvement in survival compared to RT alone. Following this report, this regimen has become the standard of care for NPC in North America. However, 3 issues must be addressed: (i) only 41% of the patients have WHO III histology (undifferentiated carcinoma) whereas >90% of our patients in Hong Kong is of this type, (ii) the control arm of RT alone gives only 24% progression free survival which is way below our

RT alone results in Hong Kong even in those years, implying that the additional gain of chemotherapy in that study is much less applicable in our locality, (iii) only 55% of the patients actually have completed the adjuvant chemotherapy. For these reasons, many oncologists in Hong Kong and in South East Asia do not regard this regimen as the gold standard, and therefore we have been conducting several trials on our own. So far the overall experience shows that post-RT adjuvant CT is generally poorly tolerated as the patients are still suffering from the side effects of concurrent CT-RT, and this very often leads to dose reduction, non-compliance and thus resulting in questionable efficacy. Thus the value of this approach still awaits results.

In contrast, neoadjuvant CT has the advantage of starting full dose chemotherapy early, thus also treating any microscopic distant metastases up front. The general experience is that because the patients are without the side effects of RT yet, full dose CT can be delivered. The second advantage which is apparent very early on is that the CT shrinks the locoregional disease often significantly (Figs 3, 4, 5), and this helps in reducing the side effects of RT in subsequent radiotherapy treatment. Although we do need to cover the entire initial tumour volume in RT planning, the high dose region to the gross residual tumour can be smaller when it has markedly shrunken, compared to the case when a bulky tumour is present at the time of planning. This is especially important when the tumour has initially involved or infiltrated very near critical structures like the optic nerve and the brain stem. This reduction of tumour volume after neoadjuvant CT will lead to a reduced dose to these critical structures and hence decreases the late complications of treatment. The improvement in overall survival by this strategy is however still not yet quantified.

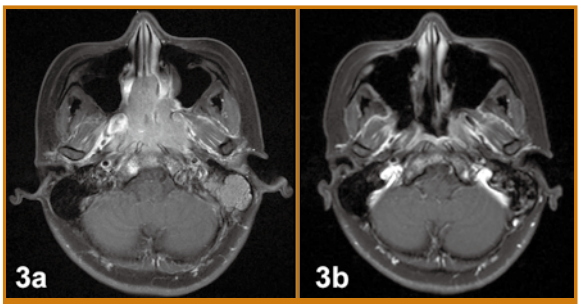

Fig 3. Effect of neoadjuvant CT on reduction of tumour volume in NP **(a)** *Pre-CT MRI of NP* **(b)** *Post-CT MRI*

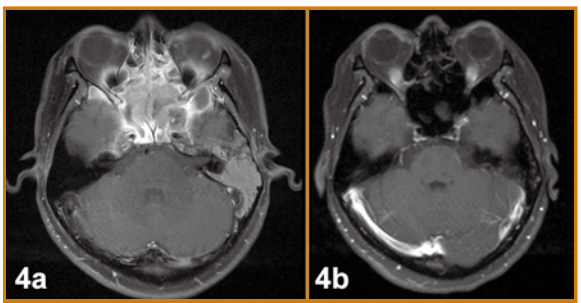

Fig 4. Effect of neoadjuvant CT on reduction of tumour invasion of sphenoid and ethmoid **(a)** *Pre-CT MRI* **(b)** *Post-CT MRI*

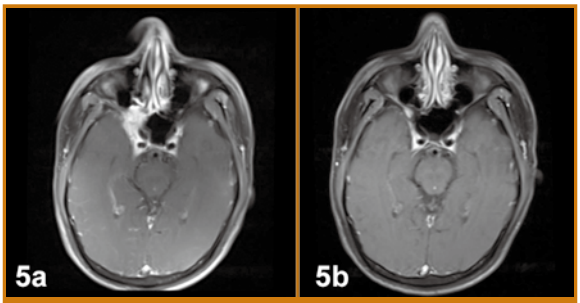

Fig 5. Effect of neoadjuvant CT on tumour invading right inferior orbital fissure and cavernous sinus **(a)** *Pre-CT MRI* **(b)***Post-CT MRI*

At present CT agents that have shown significant activity in NPC and have been used in various combinations include cisplatin, carboplatin, 5 FU, capecitabine, paclitaxel, docetaxel, and gemcitabine. The new class of targeted therapy agents has not been observed to give significant improvement in tumour control, whether alone or in combination with CT or RT and thus remains investigational in NPC.

Results

The overall treatment results as reported in various centres and trials show that the locoregional control after the primary treatment course is well over 90%. The overall survival for stage I ranges from 95-100%, stage II 80-90%, stage III 65-75%, and stage IVA/B 40-55%.

Follow Up

Follow ups after radical treatment is essential both in detecting late complications and thereby to institute corrective measures, and in diagnosing any recurrence. The family physician can encourage the patient in helping him/herself to understand that some of the side effects are transient, like alopecia, loss of taste, and skin pigmentation. Some side effects will improve significantly over time, like xerostomia with modern IMRT. Along this line, dental complications may be less nowadays but patients should be reminded to attend regular dental checks and cleaning procedure. Any infection of the ear must be treated promptly to avoid the detrimental complications of otitis media, which is seen less often nowadays with the better IMRT technique. Deafness is also reduced by IMRT as the dose to the cochlea can be lowered, and it will be unfortunate for the patients to have hearing preserved after IMRT only to lose it with otitis media. Neck muscle exercises should be encouraged to lessen the degree of neck fibrosis and stiffness. Hormonal deficiency should be checked if clinically suspicious, as hypopituitarism may still occur with IMRT when the patient has initially advanced disease involving the sphenoid sinus or cavernous sinus, though again this is seen less commonly nowadays.

NPC is one of the rare cancers in which relapses may still be potentially curable. This is clearly proven in the case of a local recurrence in the nasopharynx, or an isolated neck node recurrence, when surgical intervention, coupled with judicious use of chemotherapy, can achieve eradication of the recurrent

disease. Even for a distant relapse, a long term disease free survival or even possibly a cure has been achieved in patients with a solitary distant metastasis such as in the lung, or even in the liver or bone, or those with oligometastases in the lungs. Thus patients should be encouraged to have regular follow ups, and to be more optimistic and less anxious as the overall cure rate of this cancer is still high, and there is effective treatment even despite a recurrence.

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Dermatological Quiz

Dermatological Quiz

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Private dermatologist

Dr. Lai-yin Chong

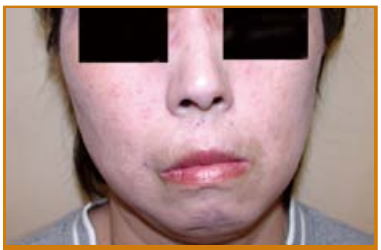

Fig. 1a: Face with malar telangiectasia, peaked nose and perioral rhagades

Fig. 1b: Hands with sclerodactyl and erythema over dorsa of phalanges

This 40-year-old female presented with Raynaud's phenomenon and skin tightening over her fingers and mouth for one year. She also had photosensitivity, polyarthralgia & myalgia. Examination showed malar rash, peaked nose and perioral rhagades (Fig.1a). There were sclerodactyl and erythema over dorsa of the phalanges (Fig.1b). Preliminary investigations showed leucopenia, elevated creatine kinase and a very high ANA titre. However, anti–Ds DNA, anti-Ro/SS-A, anti-La/SS-B, anti-centromere and anti–Scl-70 were all absent.

Questions:

1. What is your preliminary diagnosis based on the clinical and laboratory investigations?
2. What are your differential diagnoses?
3. What are the specific markers for establishing the diagnosis?
4. What is the prognosis of this disease?

(See P.32 for answers)

Dietitians' Support to Cancer Patients

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Patients diagnosed with cancer are presented with many challenges. It is estimated that up to 80% of patients with solid tumours will experience weight loss at certain stages in their disease process. For instance, pancreatic, gastric, head and neck, and lung cancers, especially in their advanced stages, are almost invariably associated with some degrees of appetite loss and muscle wasting also known as the anorexia/cachexia syndrome.[1] The success of cancer treatment is dependent on the patient's underlying health. Nutrition is an important factor in the treatment and progression of cancer.

Weight loss is a major prognostic indicator of poor survival and impaired response to cancer treatment.1 The incidence of malnutrition among patients with cancer has been estimated at between 40 and 80%.[2,3] The prevalence of weight loss in cancer patients is dependent on the tumour type, location, stage and treatment.[4] The consequences of malnutrition may include an increased risk of complications, decreased response and tolerance to treatment, hence leading to a lower quality of life, reduced survival and higher healthcare costs.[5–7] Cancer cachexia has been implicated in the deaths of 30–50% of all cancer patients.[8]

The causes of weight loss in patients with cancer are multifactorial and may be due to the symptoms reducing intake, treatment-related or mechanical obstruction or cachexia. Symptoms such as anorexia, depression, anxiety, fatigue, early satiety and pain can result in decreased appetite and food intake. Cancer treatment and its side effects may result in weight loss, for example surgery (malabsorption), radiotherapy (nausea, pain, diarrhoea, mucositis) and chemotherapy (nausea, vomiting, diarrhoea, mucositis). Weight loss may be due to mechanical obstruction caused by the cancer itself, such as obstruction of the oesophagus causing swallowing problems and reduced intake. The nutrition support to promote prompt recovery progresses after surgery and the on-going nutritional backup to retain basic health condition during the chemotherapy and radiotherapy also should be considered as the key gatekeeper.

As there are significant nutrition issues facing people with cancer, physicians are faced with the need to recognise nutrition-related issues and to implement effective strategies that will lead to positive outcomes. Nutrition is the key aspect, in which people with cancer and their carers feel that they can play an active role. Appropriate nutrition care can lead to positive patient outcomes.

Evidence-based practice guidelines for the nutritional management of cancer cachexia and nutritional management of patients receiving radiotherapy have recently been published.[9,10] These guidelines help physicians to access and utilise the best available evidence and nutrition care recommendations, which promote the multidisciplinary team and patient-centred service in clinical environments. Key aspects of the nutrition care process include identification of malnutrition, establishing the goals of treatment, determining the nutrition prescription and implementing the nutrition care.

Nutrition Treatment Goals

When setting nutrition goals and intervention options with patients and carers, it is important to present realistic potential outcomes that will be dependent on the patient's diagnosis and prognosis. Traditionally, treatment has focused on weight gain as the goal of nutrition intervention; however, weight maintenance is a more suitable goal. Several studies have demonstrated that patients with cancer who can stabilise their weight have longer survivals and improved quality of life compared with those who continue to lose weight.[11-13]

Nutrition Prescription

Energy expenditure of patients with cancer has been shown to vary greatly.[14] Treatment and disease stage may alter metabolic requirements over time. Protein intake is often reduced as the result of taste alterations, poor appetite and fatigue. Energy intake in excess of 30 kcal/kg/day and protein intake in excess of 1.4g/kg/day have been needed for weight maintenance in some studies of cancer patients.[15,16]

Eicosapentaenoic Acid

A novel approach to nutrition intervention in patients with cancer cachexia has been the prescription of eicosapentaenoic acid (EPA), an omega-3 polyunsaturated fat. Studies in both animals and humans have indicated that EPA supplementation reduces production of pro-inflammatory cytokines such as interleukin- 6, interleukin-1 and tumour necrosis factor, and in cultured cancer cell lines increases cell death rate.[17-20] Although positive changes have been demonstrated in some outcomes, including improved energy and protein intake, body composition, performance status, and quality of life in patients with cancer cachexia receiving high protein energy

supplements enriched with EPA in open trials, these results have not been confirmed in randomised trials. Studies suggested that it is important to consider issues such as compliance with the prescription,[21] duration of intervention,[22] advanced stage of cancer and the treatment group (supportive care/chemotherapy/mixed therapy) when evaluating study outcomes in future researches.

Nutrition Implementation

Nutrition implementation involves counselling the patient and/or carers to maximise food intake and facilitate optimal symptom control. Counselling, especially in conjunction with high-protein energy supplements and the techniques to show carers how to fortify the patient's favourite food in their diet, has been shown to increase intake and attenuate weight loss in a range of cancer patients. A concern expressed by many patients and carers is that consumption of high-protein energy supplements may reduce their meal intake; however, in patients with cancer, high protein energy supplements have been shown to increase intake with no negative impact on spontaneous food intake.[23,24] Prognosis, economic circumstances and client preferences need to be considered in decisions regarding supplement usage.

Nutrition counselling is effective during the phases of both active treatment (chemotherapy and radiotherapy) and supportive care. The patient's and carer's awareness on the cancer treatment and understanding of on-going nutrition support are very important; higher patient's awareness leads to a higher compliance rate. Recent studies in patients with cancer have demonstrated effective clinical outcomes with weekly to fortnightly nutrition interventions.[25-27]

Further research is required to determine the optimal therapeutic approach for cancer-induced weight loss. Future therapy for cancer cachexia is likely to be multimodal (both nutritional and pharmacological) and addresses both the reduction in food intake and metabolic alterations of the cancer patient.

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Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
★ RSCP Badminton Tournament 2013 **1**	★ The forbidden topic of men **2**	★ FMSHK Officers' Meeting ★ HKMA Council Meeting **3**	★ HKMA Golf Tournament 2013 ★ HKMA Yau Tsim Mong Community Network- Clinical Nephrology Update 2013 (Session 1) ★ HKMA Shatin Doctors Network- Managing Multiple Risk Factors in High-risk Patient Groups: An Endocrinologist's Perspective **4**	**5**	★ Joint Surgical Symposium - Hernia Surgery ★ OSHK F-symposium Focus on Osteoporosis & Fragility Fracture ★ HKMA Shatin Doctors Network- Updates on Scientific Data of Cervical Cancer Prevention and Vaccination **6**	★ HKMA CME– "You are what you eat!" & "An update on anti-aging" ★ Training Course for Medical Experts (Day 1) **7**
★ Summer Vigor Mini Dragon Boat Race ★ Training Course for Medical Experts (Day 2) ★ HKMA Badminton Tournament 2013 (Day 1) **8**	**9**	★ HKMA Kowloon West Community Network- First Session of the Certificate Course on Allergy: Paediatric Asthma in Hong Kong **10**	★ Hong Kong Neurosurgical Society Monthly Academic Meeting-Creutzfeldt Jakob Disease and Neurosurgery ★ HKMA Yau Tsim Mong Community Network- Clinical Nephrology Update 2013 (Session 2) **11**	★ HKMA Hong Kong East Community Network- From Chickenpox Vaccine to Shingles Vaccine ★ HKMA New Territories West Community Network- Importance of Overall Efficacy and Immunogenicity of Cervical Cancer Prevention Vaccines ★ HKMA Structured CME Programme with Hong Kong Sanatorium & Hospital Year 2013– Novel Treatment Option for Refractory Hypertension **12**	★ HKMA Yau Tsim Mong Community Network- Role of Primary Care Physicians in BPH Screening and Management ★ HKMA Yau Tsim Mong Community Network- Role of Primary Care Physicians in BPH Screening and Management **13**	★ HKMA CME– Refresher Course for Health Care Providers 2013/2014 **14**
★ HKMA Badminton Tournament 2013 (Day 2) **15**	★ FMSHK Presidents and Editors' Dinner 2013 **16**	★ HKMA Kowloon West Community Network– Second Session of the Certificate Course on Allergy: How to improve Pediatric Allergic Rhinitis and Asthma? ★ HKMA Tai Po Community Network- Chronic Pain Management in Osteoarthritis **17**	★ HKMA Yau Tsim Mong Community Network- Clinical Nephrology Update 2013 (Session 3) ★ HKMA Shatin Doctors Network- The Latest Treatment Option for Resistant Hypertension **18**	★ HKMA Kowloon East Community Network– Fourth Session of the Certificate Course for GPs 2013: Update on the Management of Vaginal Discharge **19**	**20**	**21**
★ RSCP Table-Tennis Tournament 2013 **22**	**23**	★ HKMA Kowloon West Community Network– Third Session of the Certificate Course on Allergy: Drug Management of COPD ★ HKMA Tai Po Community Network– Advanced Dietary Management in Heart Health and Diabetes ★ MPS Workshop– Mastering Difficult Interactions with Patients **24**	**25**	★ HKMA Hong Kong East Community Network- Hypertension Management in High-risk Population ★ MPS Workshop– Mastering Professional Interactions ★ FMSHK Executive Committee Meeting **26**	★ HKMA YTM Community Network– Osteoporosis: Current Controversies and Novel Treatment Target **27**	★ HKMA YTM Community Network- Certificate Course on Bringing Better Health to Our Community 2013 (Session 5) **28**
★ CPA Cup- National Day Celebration Dragon Boat Invitational Race 2013 ★ World Alzheimer's Day (Hong Kong Chapter)– Public Awareness Day ★ HKMA Tennis Tournament 2013 **29**	**30**					

Date / Time	Function	Enquiry / Remarks
1 SUN 1:00 pm	**RSCP Badminton Tournament 2013** Organiser: The Hong Kong Institute of Surveyors, Venue: SYS Memorial Park Sports Centre	Ms. Dorothy KWOK Tel: 2527 8285
2 MON 7:30 pm	**The forbidden topic of men** Organiser: Hong Kong Urological Association, Chairman: Dr. Simon C W WONG, Speaker: Dr. LO Ting Kit, Venue: Multi-disciplinary Simulation and Skills Centre, 4/F, Block F, QEH	Ms. Tammy HUNG Tel: 9609 6064 1 CME point
3 TUE 8:00 pm	**FMSHK Officers' Meeting** Organiser: The Federation of Medical Societies of Hong Kong, Venue: Gallop, 2/F, Hong Kong Jockey Club Club House, Shan Kwong Road, Happy Valley, Hong Kong	Ms. Nancy CHAN Tel: 2527 8898
8:00 pm	**HKMA Council Meeting** Organiser: The Hong Kong Medical Association, Chairman: Dr. TSE Hung Hing, Venue: HKMA Head Office (5/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong)	Ms. Christine WONG Tel: 2527 8285
4 WED 11:33 am	**HKMA Golf Tournament 2013** Organiser: The Hong Kong Medical Association, Chairman: Dr. HOU Lee Tsun, Laurence, Venue: HK Golf Club	Ms. Dorothy KWOK Tel: 2527 8285
1:00 pm	**HKMA Yau Tsim Mong Community Network- Clinical Nephrology Update 2013 (Session 1)** Organiser: HKMA Yau Tsim Mong Community Network, Chairman: Dr. Simon CHEUNG, Speakers: Dr. WONG Ho Sing, Joseph, Dr. Alex YU & Dr. HO Chung Ping, Venue: Block M, Lecture Theatre, Queen Elizabeth Hospital, 30 Gascoigne Road, Kowloon, Hong Kong	Ms. Candice TONG TeL : 2527 8285
1:00 pm	**HKMA Shatin Doctors Network- Managing Multiple Risk Factors in High-risk Patient Groups: An Endocrinologist's Perspective** Organiser: HKMA Shatin Doctors Network, Chairman: Dr. MAK Wing Kin, Speaker: Dr. Norman CHAN, Venue: Chairman Room, Level 2, Royal Park Hotel, 8 Pak Hok Ting Street, Shatin	Ms. Samdy CHUNG Tel : 3971 2989 Fax : 2834 0821 1.5 CME points
6 FRI 8:00 am	**Joint Surgical Symposium - Hernia Surgery** Organisers: Department of Surgery, The University of Hong Kong & Hong Kong Sanatorium & Hospital, Chairman: Dr. Michael Li, Speakers: Dr. Siu Wing-Tai & Dr. Joe Fan, Venue: Hong Kong Sanatorium & Hospital	Department of Surgery, Hong Kong Sanatorium & Hospital Tel: 2835 8698 1 CME point
12:00 noon	**OSHK F-symposium Focus on Osteoporosis & Fragility Fracture** Organiser: The Osteoporosis Society of Hong Kong, Chairmen: Prof. R Young & Dr. Law Chun Bong, Speakers: Dr. Jenny Leung, Ms. June Wong, Dr. CT Sy & Dr. Benjamin Au-yeung, Venue: Ballroom I & II, Level 7, Langham Place Hotel	
1:00 pm	**HKMA Shatin Doctors Network- Updates on Scientific Data of Cervical Cancer Prevention and Vaccination** Organiser: HKMA Shatin Doctors Network, Chairman: Dr. MAK Wing Kin, Speaker: Prof. CHEUNG Tak Hong, Venue: Jasmine Room, Level 2, Royal Park Hotel, 8 Pak Hok Ting Street, Shatin	Miss Elyse WONG Tel: 3189 8626
7 SAT 12:45 pm	**HKMA CME– "You are what you eat!" & "An update on anti-aging"** Organisers: Hong Kong Medical Association & Kowloon Hospital Alumni Society, Speakers: Ms. Wu Ching Kuen, Jenny & Dr. Chan Hau Ngai, Kingsley, Venue: Kowloon Hospital	Ms. Philippa LO Tel: 9667 5600 4 CME points
1:00 pm	**Training Course for Medical Experts (Day 1)** Organisers: Hong Kong Medical Association & Medical Protection Society, Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	HKMA CME Dept. Tel: 2527 8452 3 CME points
8 SUN 8:00 am	**Summer Vigor Mini Dragon Boat Race** Organiser: HK Amateur Dragon Boat Assn, Venue: Sai Kung	Ms. Dorothy KWOK Tel: 2527 8285
1:00 pm	**Training Course for Medical Experts (Day 2)** Organisers: Hong Kong Medical Association & Medical Protection Society, Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	HKMA CME Dept. Tel: 2527 8452 3 CME points
1:00 pm	**HKMA Badminton Tournament 2013 (Day 1)** Organiser: The Hong Kong Medical Association, Chairman: Dr. LEE Chun, Venue: MMRC	Mr. Andie HO Tel: 2527 8285
10 TUE 1:00 pm	**HKMA Kowloon West Community Network- First Session of the Certificate Course on Allergy: Paediatric Asthma in Hong Kong** Organiser: HKMA Kowloon West Community Network, Chairman: Dr. TONG Kai Sing, Speaker: Dr. TSUI Kit, Venue: Panda Grand Ballroom B, 5/F , Panda Hotel, 3 Tsuen Wah Street, Tsuen Wan, N.T.	Miss Hana YEUNG Tel: 2527 8285 1 CME point
11 WED 7:30 am	**Hong Kong Neurosurgical Society Monthly Academic Meeting-Creutzfeldt Jakob Disease and Neurosurgery** Organiser: ong Kong Neurosurgical Society, Chairman: Dr. TAN Tze Ching, Speaker: Dr. YU Chi Hung, Venue: Seminar Room, Ground Floor, Block A, Queen Elizabeth Hospital	Dr. Gilberto LEUNG Tel: 2255 3368 1.5 CME Points
1:00 pm	**HKMA Yau Tsim Mong Community Network- Clinical Nephrology Update 2013 (Session 2)** Organiser: HKMA Yau Tsim Mong Community Network, Chairman: Dr. NG Kwok Keung, Speakers: Dr. LAW Wai Ping, Dr. SIU Yui Pong, Gordon & Dr. Gensy TONG, Venue: Block M, Lecture Theatre, Queen Elizabeth Hospital, 30 Gascoigne Road, Kowloon, Hong Kong	Ms. Candice TONG Tel: 2527 8285
12 THU 1:00 pm	**HKMA Hong Kong East Community Network- From Chickenpox Vaccine to Shingles Vaccine** Organiser: HKMA Hong Kong East Community Network, Chairman: Dr. TSANG Kin Lun, Speaker: Dr. SO Man Kit, Thomas, Venue: HKMA Head Office (5/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong)	Ms. Candice TONG Tel: 2527 8285
1:00 pm	**HKMA New Territories West Community Network- Importance of Overall Efficacy and Immunogenicity of Cervical Cancer Prevention Vaccines** Organiser: HKMA New Territories West Community Network, Chairman: Dr. LEE Huen, Speaker: Dr. SO Man Kit, Thomas, Venue: Plentiful Delight Banquet, 1/F, Ho Shun Tai Building, 10 Sai Ching Street, Yuen Long	Ms. Elyse WONG Tel: 3189 8626 1 CME point
2:00 pm	**HKMA Structured CME Programme with Hong Kong Sanatorium & Hospital Year 2013– Novel Treatment Option for Refractory Hypertension** Organisers: Hong Kong Medical Association & Hong Kong Sanatorium & Hospital, Speaker: Dr. Kwok On Hing, Vincent, Venue: Function Room A, HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	HKMA CME Dept. Tel: 2527 8452 1 CME point
13 FRI 1:00 pm	**HKMA Yau Tsim Mong Community Network- Role of Primary Care Physicians in BPH Screening and Management** Organiser: HKMA Yau Tsim Mong Community Network, Chairman: Dr. CHUANG Hsin Min, Speaker: Dr. WONG Kwok Tin, Martin, Venue: Nathan Room III-Hall, Level 1, Eaton Smart, Hong Kong, 380 Nathan Road, Kowloon	Ms. Sharon LAM Tel : 3189 8787 Fax : 2597 4630 1 CME point
1:00 pm	**HKMA Shatin Doctors Network- Disease Management of Allergic Rhinitis and Rhinisinusitis** Organiser: HKMA Shatin Doctors Network, Chairman: Dr. MAK Wing Kin, Speaker: Dr. YIP Kim Kwong, Gary, Venue: Jasmine Room, 2/F, Royal Park Hotel, 8 Pak Hok Ting Street, Shatin	Ms. Samdy CHUNG Tel : 3971 2940 Fax : 2834 0821 1 CME point

Date / Time	Function	Enquiry / Remarks
14 SAT 2:15 pm	**HKMA CME– Refresher Course for Health Care Providers 2013/2014** Organisers: Hong Kong Medical Association, HK College of Family Physicians & HA-Our Lady of Maryknoll Hospital, Speaker: Dr. Wong Kam Cheung, Venue: Training Room II, 1/F, OPD Block, Our Lady of Maryknoll Hospital, 118 Shatin Pass Road, Wong Tai Sin, Kowloon	Ms. Clara TSANG Tel: 2354 2440 2 CME points
15 SUN 1:00 pm	**HKMA Badminton Tournament 2013 (Day 2)** Organiser: The Hong Kong Medical Association, Chairman: Dr. LEE Chun, Venue: MMRC	Mr. Andie HO Tel: 2527 8285
16 MON 7:00 pm	**FMSHK Presidents and Editors' Dinner 2013** Organiser: The Federation of Medical Societies of Hong Kong, Venue: Hong Kong Club, 1 Jackson Road, Central, Hong Kong	Ms. Nancy CHAN Tel: 2527 8898
17 TUE 1:00 pm	**HKMA Kowloon West Community Network– Second Session of the Certificate Course on Allergy: How to improve Pediatric Allergic Rhinitis and Asthma?** Organiser: HKMA Kowloon West Community Network, Chairman: Dr. CHAN Siu Man, Bernard, Speaker: Dr. CHAN Hing Sang, Venue: Panda Grand Ballroom B, 5/F , Panda Hotel, 3 Tsuen Wah Street, Tsuen Wan, N.T.	Miss Hana YEUNG Tel: 2527 8285 1 CME point
1:45 pm	**HKMA Tai Po Community Network- Chronic Pain Management in Osteoarthritis** Organiser: HKMA Tai Po Community Network, Speaker: Dr. Wong Kar Fai, Richard, Venue: Chiu Chow Garden Restaurant, Shop 001-003, 1/F, Uptown Plaza, No. 9 Nam Wan Road, Tai Po	Mr. Alberto NG Tel : 3929 4606 1 CME point
18 WED 1:00 pm	**HKMA Yau Tsim Mong Community Network- Clinical Nephrology Update 2013 (Session 3)** Organiser: HKMA Yau Tsim Mong Community Network, Chairman: Dr. CHAU Ka Foon, Speakers: Dr. YUNG Chee Unn, Jonathan, Dr. CHAN Ho Wong & Dr. HO Chung Ping, Venue: Block M, Lecture Theatre, Queen Elizabeth Hospital, 30 Gascoigne Road, Kowloon, Hong Kong	Ms. Candice TONG Tel : 2527 8285
1:00 pm	**HKMA Shatin Doctors Network- The Latest Treatment Option for Resistant Hypertension** Organiser: HKMA Shatin Doctors Network, Chairman: Dr. MAK Wing Kin, Speaker: Dr. LI Siu Lung, Steven, Venue: President Room, Level 2, Royal Park Hotel, 8 Pak Hok Ting Street, Shatin	Ms. Peggy LAM Tel : 9260 0274 1.5 CME points
19 THU 1:00 pm	**HKMA Kowloon East Community Network– Fourth Session of the Certificate Course for GPs 2013: Update on the Management of Vaginal Discharge** Organiser: HKMA Kowloon East Community Network, Chairman: Dr. Danny MA, Speaker: Dr. WONG Kit Wah, Angel, Venue: East Ocean Seafood Restaurant, Tseung Kwan O	Ms. Cordy WONG 3513 3087 1 CME point
22 SUN 9:00 am	**RSCP Table-Tennis Tournament 2013** Organiser: The Hong Kong Institute of Architects, Chairman: Dr. KOO Hok Tin, Hilton, Venue: Cornwall Street Sports Centre	Ms. Dorothy KWOK Tel: 2527 8285
24 TUE 1:00 pm	**HKMA Kowloon West Community Network– Third Session of the Certificate Course on Allergy: Drug Management of COPD** Organiser: HKMA Kowloon West Community Network, Chairman: Dr. LEUNG Gin Pang, Speaker: Dr. LAW Tse Sam, Grace, Venue: Panda Grand Ballroom B, 5/F , Panda Hotel, 3 Tsuen Wah Street, Tsuen Wan, N.T.	Miss Hana YEUNG Tel: 2527 8285 1 CME point
1:00 pm	**HKMA Tai Po Community Network– Advanced Dietary Management in Heart Health and Diabetes** Organiser: HKMA Tai Po Community Network, Speaker: Dr. SHEK Suk Ling, Cecilia, Venue: Chiu Chow Garden Restaurant, Shop 001-003, 1/F, Uptown Plaza, No. 9 Nam Wan Road, Tai Po	Ms. Kate NG Tel : 6323 7932 1.5 CME points
6:30 pm	**MPS Workshop– Mastering Difficult Interactions with Patients** Organisers: Hong Kong Medical Association & Medical Protection Society, Speaker: Dr. Cheng Ngai Shing, Justin, Venue: Eaton Hotel	HKMA CME Dept. Tel: 2527 8452 2.5 CME points
26 THU 1:00 pm	**HKMA Hong Kong East Community Network- Hypertension Management in High-risk Population** Organiser: HKMA Hong Kong East Community Network, Speaker: Dr. LEUNG Tat Chi, Godwin, Venue: HKMA Head Office (5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong)	Ms. Candice TONG Tel : 2527 8285
6:30 pm	**MPS Workshop– Mastering Professional Interactions** Organisers: Hong Kong Medical Association & Medical Protection Society, Speaker: Dr. Hau Kwun Cheung, Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong	HKMA CME Dept. Tel: 2527 8452 2.5 CME points
8:00 pm	**FMSHK Executive Committee Meeting** Organiser: The Federation of Medical Societies of Hong Kong, Venue: Council Chamber, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Nancy CHAN Tel: 2527 8898
27 FRI 1:00 pm	**HKMA YTM Community Network– Osteoporosis: Current Controversies and Novel Treatment Target** Organiser: HKMA YTM Community Network, Chairman: Dr. LAM Tzit Yuen, David, Speaker: Dr. WAN Man Choi, Martin, Venue: Nathan Room III-Hall, Level 1, Eaton Smart, Hong Kong, 380 Nathan Road, Kowloon	Ms. Sharon LAM Tel : 3189 8787 1 CME point
28 SAT 1:00 pm	**HKMA YTM Community Network- Certificate Course on Bringing Better Health to Our Community 2013 (Session 5)** Organiser: HKMA YTM Community Network, Speakers: Dr. YEUNG Yat Wah, Dr. LAW Tung Chi & Dr. LI Yim chu, Venue: Block M, Lecture Theatre, Queen Elizabeth Hospital, 30 Gascoigne Road, Kowloon, Hong Kong	Ms. Noel AU YEUNG Tel: 2958 8608
29 SUN 9:00 am	**CPA Cup- National Day Celebration Dragon Boat Invitational Race 2013** Organiser: Hong Kong Institute of Certified Public Accountants, Chairman: Dr. YAM Chun Yin, Abraham, Venue: Shatin Riverside	Ms. Dorothy KWOK Tel: 2527 8285
	World Alzheimer's Day (Hong Kong Chapter)– Public Awareness Day Organiser: The Hong Kong Medical Association & Hong Kong Alzheimer's Disease Association, Chairmen: Dr. CHAN Yee Shing, Alvin & Dr. CHOW Pak Chin, JP, Venue: Citywalk 2, Tsuen Wan	Miss Irene GOT Tel: 2527 8285
8:00 pm	**HKMA Tennis Tournament 2013** Organiser: The Hong Kong Medical Association, Chairman: Dr. CHIN Chu Wah, Venue: Kowloon Tong Club	Ms. Dorothy KWOK Tel: 2527 8285

Upcoming Meeting

8-10/11/2013	**International Scientific Congress- Manpower needs in medicine: moving with the times** Organiser: Hong Kong Academy of Medicine, Venue: Academy Building, Enquiry : Secretariat Tel: 2871 8787

Answers to Dermatological Quiz

Answers:

1. Mixed connective tissue disease (MCTD), which comprises overlapping features of systemic sclerosis (SSc), systemic lupus erythematosus (SLE), and polymyositis, is the most likely preliminary diagnosis. MCTD has a female predominance (F:M=4:1) and a strong association with HLA-DR4 (52%). Patients usually present with Raynaud's phenomenon. During the course of the disease, other typical features of SLE and/or SSc may develop.

2. Systemic sclerosis (SSc) and systemic lupus erythematosus (SLE) are the main differential diagnoses in this patient.

3. Anti-U1-RNP (ribonucleoprotein) and anti-U1-70kd snRNP (small nuclear ribonucleoprotein) are specific markers of MCTD. A high titre of speckled pattern fluorescent antinuclear antibody (FANA) is also typical. However, lupus-specific antibodies (such as anti-Ds DNA antibodies) and scleroderma-specific antibodies (such as anti-centromere, anti-Scl-70 (topoisomerase), and anti–PM-1 (Pm-Scl) are usually absent. Other laboratory findings include elevated creatine kinase, aldolase, leucopenia and thrombocytopenia.

4. In general the prognosis of MCTD is better if there is only one form of overlapping disease present. Renal involvement only occurs in about 5% of the cases and neurological involvement is rare. Nevertheless, many patients will progress to scleroderma or lupus, though some will remain undifferentiated. It is more severe in children as cardiac and renal involvements are more common than adults. Thrombocytopenia, which is unusual in adults, may be severe in children. Nephritis and pulmonary involvements (such as interstitial lung disease and pulmonary hypertension) are associated with a poor prognosis and are common causes of death.

Dr. Lai-yin Chong
MBBS(HK), FRCP(Lond, Edin, Glasg), FHKCP, FHKAM(Med)
Private dermatologist

HONG KONG SANATORIUM & HOSPITAL

LI SHU PUI SYMPOSIUM 2013

RECENT ADVANCES IN MEDICAL PRACTICE

Date : 15 September 2013 (Sunday)
Venue : Ballroom, JW Marriott Hotel Hong Kong

08:50 – 09:00	Welcome		Dr. Walton LI
09:00 – 09:30	**Keynote Lecture 1:** The Right Doctor for the Right Procedure		Dr. Joseph CHAN
	Symposium 1 Precise and Less Invasive Procedures	Chairperson	Dr. William WEI | Dr. Vincent KWOK
09:30 – 09:45	Cardiac Intervention		Dr. Duncan HO
09:45 – 10:00	Application of Robot in General Surgery		Dr. Michael LI
10:00 – 10:15	Makoplasty – Optimal Option of Joint Replacement		Dr. Stephen WU
10:15 – 10:30	Endoscopic Surgery for the Oesophagus		Prof. Simon LAW (HKU)
10:30 – 10:40	Q & A		
10:40 – 11:00	Coffee Break		
	Symposium 2 Diagnostics	Chairperson	Dr. LAI Kar Neng | Dr. WONG Wai Sang
11:00 – 11:15	Ultrasound in Head & Neck Medical Practice-Is There a Limit?		Prof. Anil T. AHUJA (CUHK)
11:15 – 11:30	Bronchoscopy and Beyond		Dr. LAM Bing
11:30 – 11:45	How Would Prenatal Diagnosis Make a Difference in Modern Obstetrics?		Dr. Danny LEUNG
11:45 – 12:00	Updates on Digestive Endoscopy – Diagnosis and Treatment		Dr. Angus CHAN
12:00 – 12:10	Q & A		
12:10 – 13:00	**Li Shu Pui Lecture** **How MR is Changing Medical Decisions**	Chairperson	Dr. Gladys LO **Prof. Dieter ENZMANN (UCLA)**
13:00 – 14:00	Lunch		
	Symposium 3 Genetics	Chairperson	Dr. Edmond MA | Dr. Raymond LIANG
14:00 – 14:15	Gems and Caveats of Next Generation Sequencing in Molecular Diagnosis		Dr. Chris CHAN
14:15 – 14:30	Paediatric Genetics – All About the "Next Generation"		Dr. Brian CHUNG (HKU)
14:30 – 14:45	An Update on Hereditary Breast Cancer		Dr. Ava KWONG (HKU)
14:45 – 14:55	Q & A		
14:55 – 15:25	**Keynote Lecture 2 : Liver Surgery in Private Hospital**		Dr. FAN Sheung Tat
15:25 – 15:45	Coffee Break		
	Symposium 4 GP Forum	Chairperson	Dr. Billy CHIU | Dr. CHAN On On
15:45 – 16:00	Corneal Transplant – Indications & Results		Dr. Arthur CHENG
16:00 – 16:15	Modern Oncology Treatments		Dr. KWAN Wing Hong
16:15 – 16:30	Contemporary Dental Implant Therapy – An Immediate Solution		Dr. Alfred LAU
16:30 – 16:45	Allergen Desensitization		Dr. LEE Tak Hong
16:45 – 17:00	PET for Non Malignant Diseases		Dr. Garrett HO

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參考資料: 1. Evista Prescribing Information, Hong Kong. April, 2013. 2. Cauley JA., et al. Breast Cancer Research and Treatment 65: 125—134, 2001. 3. Jaime KJ et al. Arq Bras Endocrinol Metabol. 2010 March ; 54(2): 200—205.