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Cardiology

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References: 1. Kahn S, Haffner S, Heise MA, *et al*. Glycemic durability of rosiglitazone, metformin, or glyburide monotherapy. *N Engl J Med* 2006;355:2427–443.

Please refer to the AVANDAMET Prescribing Information on page 3 for contents, indications, dosage, administration, contraindications, special precautions, adverse reactions, drug interactions, and use in pregnancy.

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The Cover Shot

"At the Window"

The picture was taken with Hasselblad SWC/M on Ilford Delta 400 Pro and scanned with Nikon coolscan LS-9000ED.

A semi-circular "turret" space in the private library of Professor Dachling Pang, a renown paediatric neurosurgeon in San Francisco.

The House was built in 1883 by a wealthy German immigrant. The style of the house is "Queen Anne", one of three classic styles in Victorian West Coast Americana architecture. The chairs are Malabar chairs from India. To your left is a Victorian Standing desk, similar to the one favoured by Winston Churchill at Chartwell mansion, Kent. To your right is the corner of a Georgian mahogany desk from England. The table lamp is a converted railway signal lamp from the early 19th centuary, also from Britain. Circular rug is from Persia.

This part of the library of Dr Pang gives me a sense of secluded serenity. 21st century San Francisco is seemingly fended off from the interior which represents more of a slice of the 19th century, of course apart from the Snoopy in the shade which is very much of the last century.

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Editorial

Dr. Bernard BL Wong

MB BS(HK), MRCP(UK), FHKCP(HK), FHKAM(Medicine), DME(Ireland), DCH(London)
Editor

Dr. Bernard BL Wong

Thank you very much to the editorial board, the Federation of Medical Societies of Hong Kong, I am more than happy to re-join the Hong Kong Medical Diary again as a cardiology issue editor since February, 2007. This is really a great honour to me and my elite team of cardiologists. In the past 2 years, because of the huge market drive and the magnificent advancement in medical and interventional technologies, numerous important landmark papers have been published. A lot of real "Changes" in our cardiovascular preventive, medical and interventional guidelines and daily practices have been going on and on.

In this issue, I am very happy that we are having a marvelous team of practical, innovative, experienced, energetic and famous cardiologists. Throughout the past decades, all of them, as my dearest friends and teachers, they really taught me a lot. They are Dr. Chan Cham Fai, Dr. Chen Wai Hong, Dr. Lee Pui Yin Clement, Dr. Leung Tat Chi Godwin, Dr. So Yui Chi and Dr. Yip Shing Biu Alex.

We are going to cover very practical topics from chest pain to arrhythmic symptoms from medicine to angioplasty intervention and from congestive heart failure to sudden cardiac death management. Our aim is to make lives easier, to simplify the confusing and difficult international updated statements and guidelines, to write them down in easy and simple points for all our dearest family practice and non-cardiology specialty colleagues.

In the middle of this "Financial Tsunami", if this cardiology issue of the Hong Kong Medical Diary can in some day and some way help you and your patients to live healthier, easier and happier, then our wish was fulfilled.

Wish you all a prosperous, healthy and happy Chinese New Year!

"Philosophy is written in this grand book, "the Universe", which stands continually open to our gaze, but it cannot be understood unless one first learns to comprehend the language and to interpret the characters in which it is written.

Galileo Galilei (1564 - 1642)

A New Look in 2009

Dr. Chun-on Mok

Editor-in-Chief

Dr. Chun-on Mok

2009 would certainly be a difficult year for some people. The Hong Kong Medical Diary would like to lighten your heart by giving a new look in the new year. Every month, we will select a photo from our colleagues as the "Cover Shot". Thanks to our President, Dr. Dawson Fong, he has invited us into his world of secluded serenity in a Victorian House and also shared with us the 19th Century antique furniture in his picture. In this issue of "Cardiology", I hope the readers can find a moment of relaxation from watching this elegant picture and help to unwind from their constant demands of medical work. This may help to bring down your blood pressure as well.

Despite the difficult economic situation, the Hong Kong Medical Diary has worked hard to improve. In the year 2009, we will increase the circulation to 8500 copies in Hong Kong. We certainly welcome a greater variety of articles on hobbies, life- styles and travel from our colleagues. Adding more spices and flavor to a medical periodical would certainly give our readers a more balanced well-being.

Finally, on behalf of the Editional Board of the Hong Kong Medical Diary, I wish you a happy and fruitful year of 2009.

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Reference : 1. Global IMS data Q1 2008. **Detailed prescribing information is available upon request.**

Chest Pain - A Guide to Our Daily Clinical Practice

Dr. Bernard BL Wong

MB BS(HK), MRCP(UK), FHKCP(HK), FHKAM(Medicine), DME(Ireland), DCH(London)

Dr. Bernard BL Wong

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 one CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 31 January 2009.

When written in Chinese, the word "crisis" is composed of two characters - one represents danger, and the other represents opportunity."

~ John F Kennedy (1917 -1963)

Chest pain is one of the most common and important presenting symptoms in our daily clinical visits.

On the surface of Planet Earth, there are 13.2 million Homo sapiens suffering from ischaemic heart disease. The number of sufferers is still increasing, by a rate of 1.2 million more per year. [1]

In the United States, there are 7 million chest pain visitors to the ER (Emergency Room) per year. 15-25% of these chest pain sufferers are real cases of acute coronary syndrome (ACS - unstable angina or acute myocardial infarction). Unfortunately, 2% of these ACS sufferers were discharged with their diagnosis missed by our ER colleagues. The mortality rate of the missed cases is two times more than those admitted.[2]

In the United Kingdom, 5% of men and 4% of women have or have had angina. There are a total of 320,000 chest pain consultations for the NHS (National Health Service) every year.[3]

In Hong Kong, heart disease is the second killer since 1960's. There were 5,169 citizens killed by heart disease in 2006'.[4] For Hospital Authority admissions under the diagnosis of ischaemic heart disease (Arrhythmia, congestive heart disease and myocardial infarction were excluded. Many of them were also caused by ischaemic heart disease), there were 17,523 admissions in 2003. In other words, there were about 48 ischaemic heart disease admissions every day.[5]

In this article, I will discuss the following topics in a simple and practical way:

1. What are the causes of chest pain and how to differentiate them clinically?
2. What are the investigations and how useful they are? &
3. Local chest pain management guidelines for Family Doctors - my humble suggestions (with reference to the updated ACC/AHA Guidelines).

Moreover, I will go through the key messages again in my favourite topic - "In a Nutshell" before the end.

Because of the limited space in this issue of the Hong Kong Medical Diary, for those who want to read more on the pathophysiology, medical and interventional management of ischaemic heart disease, please kindly go to the web site, http://www.hkma.org/chinese/cme/cme.htm. You can download my articles (free of charge) in the Hong Kong Medical Association CME Bulletin:

Ischaemic Heart Disease - A Guide to Clinical Practice

Part I	Issue July 2006'
Part II	Issue August 2006
Part III	Issue September 2006.

Once again, I sincerely hope that this article is simple, easy and useful for your daily clinical practice.

What are the Causes of Chest Pain and How to Differentiate Them Clinically?

William Heberden (1710-1801) was the first doctor to recognize and to describe angina pectoris in detail. Actually, apart from the pain character, he had no idea of any relationship between angina and the heart.[6] 100 years later, James Bryan Herrick (1861-1954) presented his landmark paper "Modern Concept of Coronary Thrombosis and Myocardial Infarction" before the Association of American Physicians in 1912. He marked the dawn of the important modern concept of coronary thrombosis and myocardial infarction. [6]

The keys for the clinical differentiation of chest pain and discomfort are:

1. Character
2. Location
3. Precipitating Factors

We can simply classify the major differential diagnoses for chest pain and discomfort as below:

1. Cardiac
2. Vascular
3. Pulmonary
4. Gastrointestinal
5. Musculoskeletal
6. Infectious
7. Psychological

The following Table 1 is very simple, straight forward and useful for clinical use:

Table 1

System	Syndrome	Clinical Description	Key differentiation Features
Cardiac	Angina	Character: pressure, burning, heaviness, for 1 -3 mins Location: Retrosternal, Radiation to neck, jaw, epigastrium, shoulders, left arms (ulnar side)	Precipitated by: full stomach, exercise, cold weather, emotional stress
	Unstable angina	As above, more severe	3 -20 mins in duration Low exercise tolerance
	Myocardial Infarction	As above, more severe	Sudden onset, > 30mins in duration, Associate with SOB, Dizziness, Sweating, nausea, vomiting, peri/syncope
	Pericarditis	Sharp, Pleuritic pain, aggravate by change in position, swallowing, breathing, variable duration, may locate in shoulders, neck, back, upper abdomen	Pericardial friction rub
Vascular	Aortic Dissection	Excruciating, ripping pain, sudden onset, anterior (ascending), radiate to back (desending)	Very severe pain, In patients with hypertension, pregnancy, Marfan Syndrome
	Pulmonary Embolism	Sudden SOB, pleuritic pain (pulmonary infarct), substernal pain (pulmonary artery distention),	SOB, Tachycardia, right heart failure
	Pulmonary Hypertension	substernal pain with exertion	SOB, right heart failure
Pulmonary	Pleuritis &/or pneumonia	Pleuritic pain, short duration, over involved area	Lateral, with SOB
	Tracheobronchitis	Mid-line Burning	coughing
	Pneumothorax	Sudden, unilateral, pleuritic, SOB	Sudden pain and SOB
Gastrointestinal	Oesophageal reflux	Burning substernal and epigastric discomfort 10-60mins in duration	Precipitated by large meal and postprandial lying down, relieved by antacid
	Peptic ulcer	Prolonged epigastric and substernal burning 60-90mins after meals	Relieved by antacid and food
	Gallbladder Disease	Prolonged epigastric, RUQ pain	Following meal
	Pancreatitis	Prolonged, intense, epigastric and substernal burning	Associated with alcohol, hypertriglyceridaemia
Musculoskeletal	Costochondritis	Sudden, intense, sharp, pin-prick, stabbing, Fleeting (Tietze syndrome)	Reproduced by pressure over affected joint
	Cervical Spinal Disease	Sudden, fleeting pain	Reproduced by neck movements
	Rib Trauma/Strain	Constant pain	Reproduced by palpation or movement of chest wall or arms
Infectious	Herpes Zoster	Prolonged burning pain in dermatomal distribution	Vesicular rash in dermatomal distribution, day 1 - day 2 after pain onset
Psychological	Panic disorder	Chest tightness, associated with dizziness, SOB, Limb & circumoral numbiness, great fear of but never suffering from "LOC and dying"	Symptoms of Anxiety, Anxiety depression

Apart from my table above, there are two very simple but useful guidelines for your daily clinical use.

1. National Heart Attack Alert Programme 1994[7]

Chief Complaints that indicate the immediate need of medical & cardiac care:

- Chest pain, pressure, tightness or heaviness; pain that radiates to neck, jaw, shoulders, back, or one or both arms
- Indigestion or heartburn; nausea and/or vomiting associated with chest discomfort
- Persistent shortness of breath
- Weakness, dizziness, lightheadedness, loss of consciousness

2. ACC/AHA Guidelines Update for The Management of Patients with Unstable Angina and Non-ST-segment Elevation Myocardial Infarction-2002[8]

Pain not characteristic of angina

- Sharp/knife - like pain with respiration/cough (Pleuritic Pain)
- Primary mid/lower abdominal discomfort
- Pain can be localised at the tip of one finger, especially over the left ventricular apex

Moreover, chest pain in women is more difficult to assess even with non-invasive tests. Very careful history and risk assessment are our key to success.

Before thinking about investigations, before reaching a definite diagnosis, before the planning of immediate management and before thinking about the prognosis..., we must first ask ourselves the followings three life saving questions:

1. What is the clinical stability of the patient?
   - Does the patient need immediate resuscitation for circulatory and/or respiratory collapse?
   - If the answer is Yes
   - Advanced Cardiac Life Support (ACLS) / Basic Cardiac Life Support (BCLS) in your clinic then,
   - Transfer the patient to a private/public hospital as soon as possible.

If the patient is clinically stable, then ask...

2. What is the immediate prognosis of the patient?
   - What is the risk that the patient is suffering from life-threatening conditions, eg. ACS, aortic dissection, pulmonary embolism?
   - If is answer is Yes again...
   - Transfer to a private/public hospital as soon as possible

3. What is the degree of the safety of referral
   - If the risk of life-threatening conditions are low, would it be safe to discharge the patient for

- private specialist (may need to wait for hours to days) or
- public specialist (may need to wait for days up to years) or
- should we (as a family doctor) directly refer the patient for further investigation and /or observation to guide for further management?

What Are The Investigations and How Useful They Are?

In this short session, we are going to talk about the indications, pros and cons for:

- ECG
- Serum Cardiac Markers
- Treadmill Stress ECG Examination
- Imaging Modalities

Electrocardiogram (ECG)

ECG is one of the oldest but still useful investigation in the world of cardiology. The first commercial ECG machine model was sold exactly one hundred years ago, in 1908, by the Cambridge Scientific Instrument Company of England.[6]

ECG is the least expensive, least technically challenging (can be easily performed by nurses and technicians) and fastest "Point - of - Care" test (can be performed swiftly, on-site, within 3 minutes). Compared with the newer investigation modalities, ECG is of course, not as sensitive and specific.

According to the AHA-ACC Statement 2004' 12-leads resting ECG should be obtained within 10 minutes of presentation in a patient with on-going chest pain.[9] There are a lot of individual differences between resting ECGs. Old ECG is always extremely useful for comparison.

The following very robust data mark the importance & usefulness of resting ECG:

- For patients with ≥1mm New ST elevation, 80% of them are suffering from acute myocardial infarction.
- For patients with New ST depression / T inversion, 20% of them are suffering from acute myocardial infarction.
- For patients with No ischaemic changes
    - In patients with past medical history of ischaemic heart disease, 4% of them are suffering from acute myocardial infarction
    - In patients without past medical history of ischaemic heart disease, only 2% of them are suffering from acute myocardial infarction[10]

In view of the above, my humble suggestion is, all family doctors should purchase an ECG machine (the most money-valued ones only cost a few thousands Hong Kong dollars) for their clinics.

One last important word on ECG, ECG is unfortunately, one of the most common arenas for malpractice, human lives and medico-legal losses because of:-

- failure to obtain an ECG on a chest pain patient,
- failure to correctly interpret the ECG obtained and most catastrophically,
- discharge the patient with an abnormal ECG home, without the indicated further evaluation and management[10]

Blood Tests

Currently, there are 2 standard blood tests for acute coronary syndrome, Cardiac Troponin (I & T) and CKMB. Please kindly forget the old tests, SGOT, LDH, and CK, for they are no longer recognised as useful cardiac markers.

Cardiac Troponin I & T[8]

- Preferred 1st line cardiac markers because of higher specificity (ACC/AHA/ESC)
- No practical difference between I & T
- An indicator of poorer prognosis even in the presence of normal CKMB
- "Point of care" bedside test, result can be available in 15 mins; for laboratory test, result can be available in 30 -45 mins,
- Inexpensive, cost less than a few hundred Hong Kong dollars per test
- If first set of blood is negative, repeat the test 6 - 12 hours later, if still negative, the negative predictive value is extremely high (>95% sensitivity and specificity)

CKMB (mass) [8]

- Serves as an alternative test to Troponin, if Troponin test is not available
- In A&E with chest pain, sensitivity 34%, specificity 88%
- Within 4 hours of chest pain onset, sensitivity <25%,
- More then 12 hours of chest pain onset, sensitivity 70 - 90 %
- CKMB can be false positive in patients with
    - Muscular dystrophy
    - High performance athletics
    - Rhabdomyolysis
    - Alcoholics
    - Trauma

One vital point, all blood tests must be ordered and interpreted with careful consideration within the whole clinical context (This is universally true for all sorts of investigations. If you are interested, please read the Bayesian Principle):

- A normal test result in a patient with high clinical probability of ACS does not exclude the diagnosis;
- Patients with very low probability of ACS should not undergo the tests because of the possibility that false positive results will lead to unnecessary hospitalisations, tests, procedures and their complications

Treadmill Exercise Stress ECG Examination[11]

Treadmill examination is the most widely used, inexpensive (just costs you about one thousand something up to a few thousand Hong Kong dollars, depending on the level of expertise), non-invasive and quick test (results can be obtained within 20 minutes!) in the world of cardiology.

The following chest pain patients with low clinical risk can safely undergo exercise testing within 6 to 12 hours or even immediately:

- 2 sets of normal cardiac markers at 4 hours interval
- Normal ECG at presentation and pre-exercise examination

- Absence of resting ECG abnormality that precludes accurate exercise ECG assessment (for example, LBBB)
- Since clinical presentation, the patient:
  - remains asymptomatic
  - with improving chest pain symptoms
  - with persistent atypical chest pain symptoms
- Absence of typical ischaemic chest pain at the time of exercise testing[12]

Treadmill stress ECG examination provides reliable prognostic information for low risk patients with test performed within 48 hours of clinical presentation:

- Positive or equivocal examination result→15% six month event rate
- Negative examination result→2% six month event rate11

Treadmill stress ECG examination is very safe. In my over 15 years' experience (Lucky?!), I do not have a single case of morbidity and mortality for my chest pain patients. Still, there are some contraindications that need to be observed carefully:

- New or evolving resting ECG abnormalities
- Abnormal Cardiac blood markers
- Inability to perform treadmill exercise (neurological and lower limb musculoskeletal disease)
- Worsening of chest pain symptoms since presentation
- Clinical risk profiling indicating imminent coronary angiography is indicated[12]

Imaging Tests

Imaging tests are good for chest pain patients who cannot perform treadmill stress ECG examination or their resting ECG abnormality affecting the accuracy of Treadmill ECG interpretation (for example. LBBB)

- Resting Echocardiogram
- Stress Echocardiogram (Exercise/Dobutamine)
- Nuclear Myocardial Perfusion Scan (Resting + Stress)
- CT coronary angiogram
- MRI myocardial perfusion and anatomy scan

In general they have the following characteristics:

- More sensitive and specific
- Ability to quantify the degree and extent of ischaemia
- Expensive (From a few thousand to over ten thousand Hong Kong Dollars per each examination)
- Invasive (except resting echocardiogram)
- Less readily available

Each test is different in their strong and weak areas, price, indication and the degree of invasiveness. The technology is also advancing in light speed. New data keep popping up every month. I would like to sincerely ask my family practice colleagues to consult their cardiologist friends before booking.

Local Chest Pain Management Guidelines for Family Doctors

~ My Humble Suggestions (With Reference to the Updated ACC/AHA Guidelines 2002').

This following is my favourite table. I have modified it from the AHA/ACC statement for our local use. It can help you to point out the likely signs and symptoms towards or the likelihood of ACS (unstable angina and acute mycocardial infarction)[13]

Table 2

Features	High likelihood (Any of the Following)	Intermediate Likelihood (Absence of High-Likelihood Features and Presence of any of the Following)	Low Likelihood (Absence of High- or Intermediate-Likelihood Features and Presence of any of the Following)
History	▪ Chest or left arm discomfort reproducing prior documented angina ▪ Hx of IHD/AMI	▪ Chest or left arm discomfort ▪ Age > 70 ▪ Male ▪ DM	Probable ischaemic symptoms in the absence of the intermmediate and high likelihood characteristics
Examination	▪ Mitral Regurgitation ▪ ↓ BP ▪ Cold Sweating ▪ Pulmonary oedema	Extacardiac vascular disease Eg. PVD, Stroke	Chest discomfort reproduced by palpitation
ECG	▪ New ST elevation ≥ 1mm ▪ New T wave inversion≥ 4mm	Fixed Q waves Old Abnormal ST segments or T waves	T wave flattening in leads with tall R waves Normal ECG
Cardiac Markers	↑ Cardiac Troponin I ↑ Cardiac Troponin T ↑ CKMB	Normal	Normal

This is my second beloved table. I have also modified it from the AHA/ACC statement for our local use. Once your diagnosis is ACS, it can help you to further risk stratify your patient. That is the likelihood of your patient, heading towards catastrophic results (Death or Nonfatal Myocardial Infarction) [13]

The Short Term Likelihood of Death or Nonfatal Myocardial Infarction in Unstable Angina Patients[13]

Table 3

Feature	High likelihood (Any of the following)	Intermediate Likelihood (Absence of High-likelihood Features & presence of any of the Following)	Low Likelihood (Absence of High- or Inermediate - likelihood Features & presence of any of the Following)
History	Accelerating tempo of ischaemic symptoms in the preceding 48hours	▪ History of MI, PVD, CVA, CABG, Aspirin usage	
Pain Character	Resting angina > 20mins	▪ resolved Resting angina > 20mins with moderate or high likelihood of CAD ▪ Resting angina < 20mins, relieved by rest/TNG	New/Progressive Canadian Cardiovascular Class III/IV angina, in past 2 weeks, without >20mins resting angina, with with moderate or high likelihood of CAD
Clinical findings	▪ Pulmonary oedema ▪ New or worsening mitral regurgitations ▪ S3/Gallop rhythm, Lung crepitations ▪ ↓ BP, ↓ HR, ↑ HR ▪ Age > 75	Age > 70	
ECG	▪ Resting angina with ST elevation > 1mm ▪ new/presumed new BBB ▪ Sustained VT	▪ T wave inversion > 4mm ▪ Q waves	Normal/Unchanged ECG during chest pain
Cardiac Markers	↑ Cardiac Troponin T > 0.1ng/ml	Slightly elevated ↑ Cardiac Troponin T > 0.01ng/ml <0.1ng/ml	Normal

The following are my humble suggestions for my dearest family practice and non-cardiac specialty colleagues:

My Tips for Management:

Once you know all the above points, the management of ACS is simple. I have 3 last tips for all my dearest family doctors:

1. For ACS patients with
   - Short Term risk of Death or Nonfatal Myocardial Ischaemia likelihood is high to intermediate:
   →immediate transfer to a private/ Hospital Authority hospital with prior notification to cardiologist/Emergency doctors, for the urgent management of ACS

2. For chest pain/angina patients with
   - Short Term risk of Death or Nonfatal Myocardial Ischaemia likelihood is low
   →refer to Private specialist (may take hours to days) / Hospital Authority Specialist Clinics (may take weeks to months), for further investigations and risk stratification

3 The most important key for success is a good history taking, meticulous physical examination, carefully selected rapid investigations with a prompt and precise management; delivered within a mutual understanding and intimate trust between patients and doctors.

In a Nutshell

1. Chest pain is a very common presentation in our daily practice
2. Heart disease is the 2nd Killer in HK
3. The key for differentiation is
   - Character
   - Location
   - Precipitating Factors
4. Before reaching a definite diagnosis, we must first ask ourselves
   - Clinical stability
   - Immediate prognosis
   - Safety of referral
5. ECG Should be obtained and interpreted within 10 mins of presentation in a patient with ongoing chest pain
6. Cardiac Troponin I & T
   - are the preferred 1st line markers,
   - if the first set of blood is negative ' repeat in 6 to 12 hours
7. Treadmill Stress ECG examination is a very useful diagnosing and risk stratification tool for low risk patients on Day 1 of presentation
8. Refer the ACS patients to a private/Hospital Authority hospital immediately for urgent management of ACS:
   - if the Short Term risk of Death or Nonfatal Myocardial Ischaemia likelihood is high to intermediate.

Every adversity, every failure and every heartache carries with it the seed of an equivalent or a greater benefit.

~ Napoleon Hill (1883 - 1970)

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Erratum

Clinical Management of COPD. Medical Bulletin 2008, vol 13, no 12 (Dec) page 7: In column 2, paragraph 3 (oxygen therapy), line 9 "LTOT should be considered for patients with COPD who have chronic respiratory failure when assessed at least twice during a stable period of 3 to 4 weeks apart, and who have an arterial oxygen tension (PaO2) of >/= 7.3kPa (54.8mmhg) or..... ". It should be "</= 7.3kPa" instead of ">/= 7.3kPa".

MCHK CME Programme Self-assessment Questions

Please read the article entitled "Chest Pain - A Guide to Our Daily Clinical Practice" by Dr. Bernard BL Wong and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded 1 CME credit under the Programme for returning completed answer sheets via fax (2865 0345) or by mail to the Federation Secretariat on or before 31 January 2009. 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. On the surface of Planet Earth, there are 13.2 million Homo sapiens suffering from ischemic heart disease.
2. Unluckily, 2% of ACS sufferers in United States were discharged with their diagnosis missed by our ER colleagues. The mortality rate of the missed cases is two times more than those admitted.
3. The keys for the clinical differentiation of chest pain and discomfort are Character, Location and Precipitating Factors.
4. Indigestion or heartburn; nausea and/or vomiting associated with chest discomfort is one of the chief complains that indicated the immediate need of medical & cardiac care.
5. Pain can be localizes at the tip of one finger, especially over the left ventricular apex is not characteristic of angina
6. For patients with No ischemic changes on ECG and without past medical history of ischemic heart disease, only 20% of them are suffering from acute myocardial infarction10
7. CKMB is the preferred first line cardiac marker for acute coronary syndrome.
8. For treadmill stress ECG examination performed within 48 hours of clinical chest pain presentation, patients with positive or equivocal examination result are going to have a 5% six month cardiovascular event rate.
9. Dobutamine pharmacological stress echocardiogram is a non-invasive imaging investigation.
10. The most important key to success is high-tech investigation and invasive management only.

ANSWER SHEET FOR JANUARY 2009

Please return the completed answer sheet to the Federation Secretariat on or before 31 January 2009 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

Chest Pain - A Guide to Our Daily Clinical Practice

Dr. Bernard BL Wong

MB BS(HK), MRCP(UK), FHKCP(HK), FHKAM(Medicine), DME(Ireland), DCH(London)

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

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Answers to December 2008 issue

Clinical Management of COPD

1.e 2.e 3.d 4.a 5.b 6.a 7.e 8.d 9.e 10.c

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†*As part of a treatment strategy to lower Total-C and LDL-C to target levels, as an adjunct to diet*

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Antiplatelet Therapy for Atherothrombotic Diseases

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Dr. Wai-hong Chen

Abstract: Atherothrombosis describes the formation of a thrombus on a disrupted atherosclerotic plaque, and is the primary cause of acute ischaemic events. Atherothrombosis is a generalised and progressive process with an inflammatory component. Patients with disease in one vascular bed are at risk of disease in another. Platelet adhesion, activation, and aggregation in the final stage of atherothromobosis are responsible for arterial occlusion and consequent ischaemia. Therefore antiplatelet therapy is an effective treatment choice for secondary prevention. Clopidogrel, an adenosine diphosphate receptor antagonist, given alone or in combination with aspirin, may benefit secondary prevention of ischaemic events. Current treatment guidelines suggest the use of combination of these two agents for secondary prevention where appropriate. However, data conflict regarding the efficacy of antiplatelet therapy for primary prevention. A recent meta-analysis demonstrated that aspirin significantly reduces the risk of first myocardial infarction in both men and women. The recent Clopidogrel for High Atherothrombotic Risk and ischemic Stabilization Management, and Avoidance trial, (CHARISMA) which evaluated the effects of clopidogrel plus aspirin compared with aspirin alone, seems to support the use of dual antiplatelet therapy in secondary prevention, but suggests that it may not be more effective than aspirin alone in primary prevention.

Key Words: atherothrombosis, aspirin, clopidogrel, antiplatelets, cardiovascular disease

Atherothrombosis, the unhealthy coupling of atherosclerosis and thrombosis, is the most common cause of acute ischaemic events. The underlying atherosclerotic process is diffuse, generalised, and progressive, affecting multiple vascular beds. This leads to a number of clinical manifestations, the natures of which are influenced by the target organ and specific vascular bed involved. Ischaemic events related to atherothrombosis include coronary, cerebral, and peripheral arterial disease (PAD).

Disease in one vascular bed increases the risk of disease in other, a concept known as "cross-risk."[2-3] In the Reduction of Atherothrombosis for Continued Health (REACH) Registry, which included a total of 67,888 patients from 44 countries, 15.9% of the 55,499 with symptomatic atherothrombosis had polyvascular disease, defined as at least 2 of the following: coronary artery disease (CAD), PAD, and cerebrovascular disease.[4] These patients, who tend to be older and have more comorbidities, had higher rates of cardiovascular outcomes after 1 year of follow-up compared with patients with vascular disease in a single bed.[5] Patients with one ischaemic event have an increased likelihood of experiencing another event in the future. A 7-year population-based study showed that, compared with patients who had no history of myocardial infarction (MI), those who had experienced a prior MI had significantly increased risks of stroke (1.9 % versus 7.2 %) and death from cardiovascular causes (2.1 % versus 15.9 %) ,in addition to an increased risk of recurrent MI (3.5 % versus 18.8 %).[6] Similarly, a community-based study of patients with a first stroke demonstrated that among those who survived the first 30 days after the initial events, other cardiovascular events accounted for approximately the same proportion of deaths (26 %) as the initial stroke (27%) during the following 10 years.[7] Secondary prevention is therefore necessary in all patients with a history of ischaemic events.

Management of ischaemic risk factors, through a combination of lifestyle modifications and pharmacotherapy, reduces the incidence of ischaemic events.[8] There are a number of pharmacological agents useful for primary and secondary prevention; this review will focus on the role of antiplatelet agents in the prevention of atherothrombotic events in patients at high risk.

Pathophysiology of Atherothrombosis

The pathogenesis of atherothrombosis is a complex process that can be divided into 5 phases, with inflammation playing a key role.[1,9,10] Indeed, atherosclerosis and atherothrombosis are currently viewed as inflammatory disorders.[11] Atherosclerotic plaque rupture heralds the activation of haemostasis, involving platelets and the coagulation system. Under the high shear flow of a ruptured plaque, platelets may adhere directly to von Willebrand factor (vWF) and the activated endothelium, initiating the process of platelet activation. Platelets undergo a series of important events during activation, including: (1) shape change from a tiny disc to sphere with extending filopodiae; (2) activation of the surface glycoprotein IIb/IIIa receptor, the ultimate path to platelet aggregation; and (3) the release of vasoactive (eg, thromboxane A_2, serotonin, platelet-activating factor), pro-aggregant [eg, adenosine diphosphate (ADP), vWF], and pro-coagulant (e.g. thrombin, tissue factor) substances from platelet granules. After initial activation, potent amplification

mechanisms, such as platelet-to-platelet aggregation and fibrin formation ensue, leading to a growing thrombus at the site of plaque rupture.

Despite this complex response, most plaque ruptures remain clinically silent, as the fibrous cap of the plaque is constantly undergoing remodelling, rupture, thrombosis, and healing.[11] Clinically manifested ischaemic events occur when acute thrombosis arises on top of plaque rupture, bringing along the ominous consequences of acute flow impairment. In the case of coronary heart disease, the type and severity of the syndrome seem to be related to the extent of vessel obstruction (whether total or partial) and the duration and severity of critical ischaemia over the threshold of myocardial sensitivity.[12]

Identification of High-Risk Patients

Individuals with evidence of atherosclerotic lesions are at risk for clinically manifested atherothrombotic events. Symptomatic patients with established coronary, cerebrovascular, or PAD are particularly at high risk for recurrent events.[2,8] We have learned in recent years that individuals with silent atherosclerosis and multiple risk factors such as hypercholesterolaemia, diabetes, cigarette smoking ,or uncontrolled hypertension are also at risk for clinically manifested ischaemic syndromes.[13] A study which compared the 7-year incidence of MI in patients with type 2 diabetes mellitus (DM) and nondiabetic subjects indicated that diabetic patients without prior history of MI are at equivalent risk of an event as nondiabetic patients with pervious MI history.6 Diabetic patients with no prior MI and nondiabetic subjects who had a history of MI at baseline had similar rates of MI (20.2% versus 18.8%), stroke (10.3% versus 7.2%), and death from cardiovascular causes (15.4% versus 15.9%) during the follow-up period. These and other high-risk groups need to be identified early, as they may be candidates for aggressive medical therapy in addition to lifestyle modification.

Oral antiplatelet Agents and Impact on Ischaemic risk Reduction

Given the central role of platelets in atherothrombosis, antiplatelet agents are an important armament in the management of atherothrombotic syndromes, whether in acute treatment or for secondary prevention.

Aspirin (N-acetylsalicylic acid) is a time-honoured, inexpensive antiplatelet agent, the most extensively studied drug of its class. Aspirin binds to and irreversibly inhibits cyclo-oxygenase (COX), the first step enzyme in the biosynthesis of prostaglandins in platelets. Pharmacologic inhibition of COX in platelets blocks the arachidonic pathway of platelet activation, effectively shutting down the formation of thromboxane (Tx) A_2, its end terminal product. Tx A_2 is a potent platelet agonist and vasoconstricting substance.[14] The irreversible inhibition of COX stems from the fact that platelets are anuclear cells, hence devoid of protein synthesis and unable to replete its pool of enzymes. The end result is a shutdown of Tx A2 production for the remaining life of the platelet, i.e., its physiologic lifespan of 10 days.

Dipyridamole is thought to inhibit phosphodiesterase, which acts as a catalyst for cyclic adenosine monophosphate (cAMP) in platelets. Increased cAMP activity diminishes calcium mobilisation from the platelet cytosol, an important step for platelet activation to ensue.[14]

Clopidogrel and ticlopidine block the ADP receptor on platelets, key to another important pathway for platelet activation and aggregation. ADP is an important constituent of the platelet granules, released during the shape change phase of activation. The released ADP provides an important amplification mechanism toward local platelet aggregation and other platelet-to-platelet interaction reactions. The situation is further compounded by the reduced activities of enzymes (endothelial ecto-ADPases) responsible for ADP degradation under physiologic conditions. Experimental models of arterial thrombosis under high shear flow conditions have underscored the salient role of ADP-induced platelet activation.[14-16]

Secondary Prevention

Antiplatelet Class

In its latest meta-analysis update, the Antithrombotic Trialists' Collaboration (ATC) group reported on the cumulative effectiveness and safety of antiplatelet agents in more than 135,000 patients from 195 trials. These studies enrolled patients at high risk for vascular events due to preexisting disease or a recent vascular event.

The pooled analysis of the general antiplatelet class, with all agents combined, yielded a highly significant 2.5% absolute reduction in the number of major vascular events (i.e., nonfatal MI or stroke, or vascular death) during the observation period (10.7% versus 13.2%; $P = 0.0001$).17 For specific outcomes, the absolute risk reductions were 1.2% (2.46% versus 3.66%) for nonfatal MI, 0.89% (2.99% versus 3.88%) for nonfatal stroke, and 1.05% for vascular mortality.[17] Antiplatelet therapy significantly reduced the risk of vascular events in patients with stroke or transient ischaemic attack (TIA), PAD, and unstable angina (UA), underscoring once again the systemic nature of atherothrombosis.

Although the analysis showed that antiplatelet therapy was associated with an absolute 0.42% excess of serious (fatal or nonfatal requiring transfusion) extracranial bleeding (1.13% versus 0.71%), this was offset by a reduction in vascular events, with an overall positive net benefit.

Aspirin Alone

Aspirin alone yielded an absolute 3.1% reduction in vascular event rates versus control (12.9% versus 16.0%). The size of the cumulative patient cohort available in the ATC meta-analysis update allowed for comparisons amongst aspirin doses, a subject of debate during the last

2 decades.[17] Aspirin dose comparisons for 75 to 150 mg, 160 to 325 mg, and 500 to 1500 mg yielded absolute reductions of 4.3%, 3.3%, and 2.7%, respectively. There is no evidence to support improved efficacy for aspirin doses > 1500mg. Doses < 75 mg yielded an absolute reduction of 2.1%. However, results for the < 75mg versus > 75 mg subgroups were not statistically significant. The risk of serious extracranial bleeding was fairly constant amongst aspirin dose < 325 mg. Overall, a daily dose of 75 to 150 mg aspirin seems to provide the best benefit-to-risk ratio.

Dipyridamole

For dipyridamole, the meta-analysis included 25 non-confounded studies which compared dipyridamole plus aspirin with aspirin alone.[17] The addition of dipyridamole to aspirin yielded a nosignificant 0.6% absolute reduction in vascular events (11.8% versus 12.4%). Results from the second European Stroke Prevention Study (ESPS-2), which enrolled patients with a history of stroke or TIA, demonstrated that although extended-release dipyridamole did not reduce the rate of recurrent stroke compared with aspirin alone, the combination was associated with an approximately 3% absolute decrease in the rate of recurrent stroke compared with either agent alone (9.5% for extended-release dipyridamole plus aspirin versus 12.8% for extended-relaease dipyridamole alone versus 12.5% for aspirin alone; P <0.001).[18] The efficacy of the combination of extended-release dipyridamole and aspirin in reducing recurrent stroke was comfirmed in the European/Australasian Stroke Prevention in Reversible Ischaemia Trial (ESPRIT).[19]

ADP-Receptor Antagonists

Ticlopidine and clopidogrel are prodrugs, inactive in vitro, activated in vivo upon hepatic conversion. Both agents inhibit ADP-induced platelet aggregation.

The proof of concept for clopidogrel was established in the Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events (CAPRIE) trial, a randomised comparison of clopidogrel 75mg and aspirin 325 mg. CAPRIE assessed the relative efficacy and safety of clopidogrel in the secondary prevention of vascular events (i.e., vascular death, nonfatal MI, ischaemic stroke, leg amputation) in 19,185 patients with a prior MI or ischaemic stroke, or with symptomatic PAD, all of which are manifestations of diffuse atherothrombotic disease.[20] Clopidogrel was associated with a significant absolute reduction of 0.51% in the rate of the primary composite endpoint of MI, ischaemic stroke or vascular death compared with aspirin (5.32% versus 5.83%; P = 0.043). Clopidogrel was associated with significantly less gastrointestinal bleeding and ulcers when compared with aspirin.

The aim of the Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) study was to evaluate the role of long-term therapy with aspirin and clopidogrel in patients at high risk for secondary cardiovascular events.[21] Patients who presented within 24 hours with UA/non-ST segment elevation (NSTE) MI were randomly assigned to receive clopidogrel (300 mg loading dose followed by 75 mg/d) or placebo in addition to aspirin (75-325 mg/d) for 3 to 12 months. Clopidogrel plus aspirin was associated with a significant 2.1% absolute reduction in the rate of the primary composite endpoint of MI, stroke, or cardiovascular death compared with placebo plus aspirin (9.3% versus 11.4%; P < 0.001), with benefits demonstrated as early as the first day. There was no significant difference in life-threatening bleeding between groups; however, significantly more patients receiving clopidogrel plus aspirin experienced major bleeding (3.7% versus 2.7%; P = 0.001), and the risk of minor bleeding was also significantly higher among clopidogrel recipients (5.1% versus 2.4%; P < 0.001). Major bleeding rates in CURE were dependent on aspirin dose. Current American College of Cardiology/American Heart Association guidelines[22] recommend at least 1 month, and ideally up to 1 year, of treatment with clopidogrel plus aspirin for patients with UA/NSTEMI.

Findings from 2 major randomised trials highlight the clinical benefits to be gained from sustained dual antiplatelet therapy after percutaneous coronary intervention (PCI).[23,24] The PCI-CURE study compared the effects of pretreatment and long-term therapy with clopidogrel versus placebo in 2,658 aspirin-treated patients from the CURE population who underwent PCI.[23] The primary composite endpoint of cardiovascular death, MI or urgent target vessel revascularisation with significantly less frequent in the clopidogrel group than the placebo group (4.5% versus 6.4%; P = 0.03). Furthermore, long-term administration of clopidogrel post-PCI was associated with a lower rate of cardiovascular death or MI between PCI and the end of follow-up compared with placebo (6.0% versus 8.0%; P = 0.047). There was no significant difference in the rates of major bleeding, including life-threatening major bleeding, within 30 days of PCI between the clopidogrel and placebo groups (1.6% versus 1.4%; P = 0.69). The Clopidogrel for the Reduction of Events During Observation (CREDO) study compared the effects of long-term (12 months) clopidogrel versus placebo therapy in aspirin-treated patients undergoing elective PCI.[24] At 12 months' follow-up, the dual antiplatelet regimen was associated with a significant 3% absolute reduction, relative to aspirin alone, in the composite endpoint of death, MI, or stroke (8.5% versus 11.5%; P = 0.02). There was no significant difference in the risk of major bleeding between the 2 groups.

Currently, evidence-based guidelines recommend that patients implanted with bare metal stents receive dual antiplatelet therapy for at least 1 month, whereas patients implanted with a sirolimus or paclitaxel drug-eluting stent (DES) receive dual antiplatelet therapy for at least 3 and 6 months, respectively.[25] The guidelines also recommend that ideally, dual therapy should be maintained for 1 year. Based on the finding the premature discontinuation of dual antiplatelet therapy is a predictor of late stent thrombosis, a recently published Science Advisory recommends that all patients implanted with a DES should receive 12 months of dual antiplatelet therapy.[26] It is further recommended that if a patient is unlikely to complete a 12-month dual antiplatelet regimen, regardless of the

reason, strong consideration should be given to implanting a bare metal stent instead.

The benefits of dual treatment can also be extended to the management of ST-segment elevation (STE) MI patients.[27-28] The question of whether the addition of clopidogrel is beneficial in patients with STEMI who are receiving a standard fibrinolytic regimen, including aspirin, was addressed in the Clopidogrel as Adjunctive Reperfusion Therpy-Thrombolysis In Myocardial Infarction Study 28 (CLARITY-TIMI 28).[28] A total of 3,491 patients who presented within 12 hours of the onset of STEMI were randomised to receive clopidogrel 75 mg/d (after a loading dose of 300mg) or placebo; all patients received fibrinolytic therapy and aspirin. The primary endpoint was a composite of an occluded infarct-related artery on angiography, or death, or recurrent MI before angiography. The rates of the primary endpoint were significantly lower in the clopidogrel than placebo group (15% versus 21.7%; $P < 0.001$). At 30 days, the rate of occurrence of the composite endpoint of cardiovascular death, recurrent MI or recurrent ischaemia requiring urgent revascularisation was reduced by 2.5% (from 14.1% to 11.6%; $P = 0.03$) in the group receiving clopidogrel. The rates of major bleeding were similar in the clopidogrel and placebo groups (1.3% versus 1.1%; $P = 0.64$). The PCI-CLARITY study, a prospective analysis of the 1,863 patients from CLARITY-TIMI 28 who underwent PCI, showed that pretreatment with clopidogrel significantly reduced the incidence of cardiovascular death, MI or stroke during the 30-day period after PCI compared with placebo (3.6% versus 6.2%; $P = 0.008$).[29] There were no significant differences in TIMI major or minor bleeding events between clopidogrel and placebo (2.0% versus 1.9%; $P > 0.99$).

The Clopidogrel and Metoprolol in Myocardial Infarction Trial/Chinese Cardiac Study (COMMIT/CCS) was designed to assess the effect of clopidogrel (75 mg/d) versus placebo in STEMI patients who were also receiving aspirin therapy (162 mg/d), for a mean treatment period of 15 days.[27] The composite primary endpoint of death, reinfarction, or stroke was significantly less frequent in clopidogrel than placebo recipients (9.2% versus 10.1%; $P = 0.002$). A significant reduction in the second primary endpoint of death from any cause was also achieved in clopidogrel recipients (7.5% versus 8.1%; $P = 0.03$). There was no significant difference in the rate of major bleeding events between the 2 groups; however, minor bleeding was significantly more common in the clopidogrel arm than the placebo arm (3.6% versus 3.1%; $P = 0.005$).

Clopidogrel is significantly more expensive than aspirin. However, a review of several pharmacoeconomic analyses revealed that dual antiplatelet therapy with aspirin and clopidogrel is cost- effective when used for up to 12 months by patients with UA/NSTEMI or coronary stents.[30]

Evidence for the efficacy of dual antiplatelet therapy in secondary prevention in high-risk patients with recent ischaemic stroke is limited. The results of the Clopidogrel and Aspirin for Reduction of Emboli in symptomatic carotid Stenosis (CARESS) trial showed that the combination of clopidogrel and aspirin was more effective than aspirin alone in reducing asymptomatic embolisation in patients with recent symptomatic carotid stenosis.[31] However, in the Management of Atherothrombosis with Clopidogrel in High-risk patients (MATCH) trial, the addition of aspirin to clopidogrel administered for up to 18 months in high-risk stroke and TIA patients conferred no extra efficacy advantage, but increased the risk of life-threatening or major bleeding compared with clopidogrel alone.[32]

Primary Prevention

The efficacy of antiplatelet therapy for primary prevention of atherothrombosis is unclear. In 1988, the US Physicians' Health Study showed that aspirin (325 mg on alternate days) reduced the absolute risk of first MI in supposedly healthy men by 0.9% (1.3% versus 2.2%; $P < 0.00001$), but did not reduce cardiovascular mortality in subjects aged > 50 years.[33] Conversely, results from the British Doctors' Trial of male subjects did not show any significant benefit of aspirin (500 mg/d) on the incidences of and mortality from stroke, MI, or other vascular conditions.[34]

A meta-analysis of 5 randomised trials of aspirin in the primary prevention of cardiovascular disease (including both US Physicians' Health Study and the British Doctors' Trial) published in 2003 showed that aspirin does significantly reduce the risk of a first MI in both men and women.[35] Among the 55,580 subjects included in this meta-analysis, aspirin was associated with a statistically significant 0.70% reduction in the rate of first MI (1.65% versus 2.35%) and a significant 0.37% reduction in the rate of all important vascular events, defined as a composite of nonfatal MI, nonfatal stroke, and vascular death (4.14% versus 4.51%). However, aspirin did not have a significant effect on the risk of either nonfatal stroke or vascular death alone. Conversely, the Women's Health Study, a large primary prevention trial in 39,876 women published in 2005, showed that aspirin 100 mg on alternate days reduced the risk of stroke without affecting the risk of MI or cardiovascular death.[39] A subsequent sex-specific meta-analysis, showed that aspirin had different effects in men and women.[40] Although aspirin therapy was found to significantly reduce the risk of major cardiovascular events (composite of stroke, MI, cardiovascular death) in both sexes, in women this was through a reduction in the rate of ischaemic stroke (0.84% versus 1.08%; $P = 0.008$), whereas in men this was due to reduction in MI (1.91% versus 2.76%; $P = 0.001$). Aspirin had no significant effect on the risk of MI in women or stroke in men, and did not significantly reduce cardiovascular mortality rates in either sex. An increased rate of major bleeding (predominantly gastrointestinal) was observed in both women (0.71% versus 0.46%; $P = 0.01$) and men (0.081% versus 0.48%; $P < 0.001$).

The US Preventive Services Task Force (USPSTF)41 found good evidence that aspirin reduces the incidence of CAD in adults who are at increased risk. The USPSTF concluded that for asymptomatic individuals whose 5-year ischaemic risk is > 3%, the benefits of long-term aspirin therapy are likely to outweigh any associated risks. However, there is currently no clear consensus on the use of aspirin or other antiplatelets for primary

prevention. Critical evaluation of the literature and use of the Framingham coronary heart disease risk prediction score sheets are, for the moment, the best tools for clinical practitioners to assess patient risk and decide upon treatment for individual patients.[42]

CHARISMA: Dual Antiplatelet Therapy for Primary and Secondary Prevention

The Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management, and Avoidance (CHARISMA) trial[43-45] evaluated the effects of dual antiplatelet therapy with clopidogrel and aspirin in a broad population of high-risk patients. The study included a total of 15,603 patients who were followed to a fixed study end date that allowed for at least 1,040 primary endpoint events (cardiovascular death, MI, or stroke) to occur. In addition to the overall population, CHARISMA evaluated the efficacy and safety of dual antiplatelet therapy for secondary prevention in 12,153 symptomatic patients with established CAD, cerebrovascular desease, or PAD, and for primary prevention in 3,284 asymptomatic patients considered to be at high risk of atherothrombotic events. To qualify as a high-risk primary prevention candidate, patients were required to have 2 major, 3 minor, or 1 major and 2 minor atherothrombotic risk factors.

Results of the CHARISMA study[44-45] suggested mixed benefits for dual antiplatelet therapy. Among the overall population, treatment with clopidogrel plus aspirin did not significantly reduce the incidence of the primary endpoint, i.e., a composite of MI, stroke, or death from cardiovascular causes (6.8% versus 7.3%; P = 0.22), but did reduce the risk of the principal secondary endpoint of first MI, stroke, cardiovascular death, or hospitalisation for UA, TIA, or revascularisation (16.7% versus 17.9%; P = 0.04).44 There was no significant difference in the rates of GUSTO-defined severe bleeding between the groups receiving clopidogrel plus aspirin or aspirin alone (1.7% versus 1.3%; P = 0.09), but moderate bleeding was more frequent with dual antiplatelet therapy (2.1% versus 1.3%; P < 0.001). Subgroup analysis of patients enrolled with a history of MI, stroke, or symptomatic PAD seems to support the use of dual antiplatelet therapy for secondary prevention in these patients as the rates of the primary endpoint decreased by 1.5% in patients taking dual therapy (7.3% versus 8.8%; P = 0.010).45 The absolute risk reductions were similar for patients enrolled with a history of MI (6.6% versus 8.3%; P = 0.031), stroke (8.4% versus 10.7%; P = 0.029), and PAD (7.65 versus 8.7%; P = 0.285). There was also no significant difference in severe bleeding between groups (1.75 versus 1.5%; P = 0.509). In contrast, among asymptomatic patients evaluated for primary prevention, treatment with clopidogrel plus aspirin did not produce a significant reduction in primary endpoint events compared with aspirin alone (6.6% versus 5.5%; P = 0.20), and a significant increase in cardiovascular death was observed with dual antiplatelet therapy in this subgroup (3.9% versus 2.2%; P = 0.01). A nonsignificant difference in the rate of severe bleeding was reported between the clopidogrel plus aspirin group and the group receiving aspirin alone (2.0% versus 1.2%; P = 0.07). Precise reasons for the difference in efficacy in the asymptomatic and symptomatic populations have yet to be elucidated.

Conclusion

Atherothrombosis is the most common cause of ischaemic events. Individuals with a history of atherothrombotic events are at high risk of recurrence and are at risk for ischaemic disease in multiple vascular beds. Many individuals with asymptomatic, clinically silent atherothrombosis are also at high risk of ischaemic events. As the platelets play a pivotal role in the process of atherothrombosis, antiplatelet agents are effective and have become well established for the secondary prevention of ischaemic events in at-risk patients.

The benefits of antiplatelet therapy in the primary prevention setting are less clear. Primary prevention was explored further in the CHARISMA study, which investigated the relative efficacy of aspirin monotherapy versus dual antiplatelet therapy with clopidogrel plus aspirin for primary prevention in patients at high risk for atherothrombosis and for secondary prevention in patients with established MI, stroke or PAD. Although results of this trial suggested that dual antiplatelet therapy may be beneficial in the secondary prevention setting and concur with major studies such as CURE and COMMIT, a similar benefit was not observed for primary prevention in asymptomatic patients. Further study of dual antiplatelet therapy is therefore warranted in symptomatic patients only.

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Updates on Percutaneous Coronary Intervention

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The past 30 years witnessed a revolution in cardiovascular care with the introduction of percutaneous approaches for the treatment of patients with a variety of cardiovascular diseases. According to overseas and local experiences, the number of percutaneous coronary intervention (PCI) performed every year far exceeds the number of patients undergoing coronary artery bypass surgery (CABG). The procedural success, safety and durability of PCI have dramatically improved because of the advance in technology, refinements in periprocedural adjunctive pharmacology (e.g. glycoprotein IIb/IIIa inhibitors, alternative thrombin inhibitors), and a better understanding of early and late outcomes. Indeed, it is now one of the most frequently performed medical procedures.

In this article, I will review a few important trials in the field of intervention cardiology.

Drug-eluting Stents (DES)

The idea of combining a coronary stent and an anti-proliferative drug is to target the different components of restenosis. By achieving a bigger post-procedural vessel lumen, the use of bare metal coronary stent reduces both clinical and angiographic restenosis. However, 20 to 30% of these patients have recurrent symptoms due to neointimal hyperplasia which is a "normal response" to vascular injury. A number of systemic agents have been used to prevent restenosis after balloon angioplasty and stenting, but none has had a consistent effect on restenosis prevention. By local delivery of a highly efficacious anti-proliferative drug, DES is very effective at suppressing the local neointimal proliferation. Angiographic and clinical restenosis in general have been reduced to less than 10% and 5% respectively. Siroliums and paclitaxel eluting stents were the first two stent platforms studied and were available in clinical use. However, new problems specific to DES were noticed. These included delayed endothelialisation, impaired arterial wall healing and late stent thrombosis. Hence, there is a need for a new DES platform and, hopefully, DES related problems and complications could be minimised.

A thin, cobalt-chromium stent eluting the antiproliferative agent everolimus from a nonadhesive, durable fluoropolymer has been developed and it has shown promise in preliminary studies in improving clinical and angiographic outcomes in patients with coronary artery disease. SPIRIT III compared this everolimus-eluting stent (EES) with a widely used paclitaxel-eluting stent (PES) in a prospective, randomised and controlled setting1. It showed less angiographic late loss (i.e. less neointimal hyperplasia which translates into less restenosis) in EES compared with PES. There were also fewer major adverse cardiac events (MACE - cardiac death, myocardial infarction, or target lesion revascularisation) during 1 year of follow-up. This was the first DES to prove superior, in a randomised clinical trial, to another DES already on the market. This EES then was granted marketing approval by the FDA in July 2008. Because this stent was more user-friendly (highly deliverable) and had favourable clinical outcomes, it had been used extensively by the US interventionist since its marketing. Similar experience was noted in Hong Kong. However, as this stent was relative new to the market, there were no long-term data in compared with the first generation DESs.

Medical Therapy vs PCI

The value of PCI for patients with disabling or unstable angina or myocardial infarction is well proven in clinical trials. Controversial, however, is the role of PCI for patients who are either asymptomatic or minimally symptomatic2,3. This issue intensified after the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial2, which randomised 2287 patients who had stable coronary artery disease to either optimal medical therapy plus PCI or optimal medical therapy (OMT) alone. After a median follow-up of 4.6 years, the primary end point (death and myocardial infarction) was almost identical between PCI (19%) and OMT (18.5%). However, a group of relatively low-risk patients were randomised: 12% to 13% were asymptomatic, whereas 30% had Canadian Cardiovascular Society class 1 angina; approximately 70% had 1- or 2- vessel disease; and the ejection fraction was 61%. Meanwhile, during the trial, 33% of the medical group crossed over to PCI whereas only 21% of the PCI group required repeat revascularisation. Moreover, in the PCI group, only balloon angioplasty was performed in 14.5% of lesions and DES was rarely used because of the time frame of the study.

An important substudy of COURAGE compared scintigraphic stress tests at 6-18 months follow-up with the baseline study in 314 patients4. Each group had similar baseline characteristics. As measured by scintigraphy, increasing amounts of jeopardised

myocardium at baseline indicated increased risk of end points. At follow-up scintigraphy, the reduction in ischaemic myocardium was greater with PCI than with OMT particularly in patients with moderate to severe ischaemia at baseline. Patients with ischaemia reduction had lower risk for death or myocardial infarction. Death or MI rates ranged from 0% for patients with no residual ischaemia to 39% in patients with 10% residual ischaemia on follow-up stress test. This supported the importance of recognition and treatment of ischaemic burden rather than just anatomy as the goal of interventional therapies.

The COURAGE study indeed reconfirmed what we are currently practising. For those patients with minimal symptom or no symptom, optimal medical therapy offers good control of symptom without increased risk of death or myocardial infarction. However, if there is significant inducible ischaemia on function test (e.g. stress scintigraphy), PCI could relief residual ischaemia and reduce cardiovascular events whether the patient is symptomatic or not. If medical therapy does not provide adequate angina relief, provide desired physical activity level to meet the patient's expectations, or the patient is intolerant of medical therapy, PCI is the treatment of choice. Last but not the least, OMT includes antiplatelet therapy (aspirin, clopidogrel), anti-ischaemic therapy (long-acting beta-blocker, long-acting calcium channel blocker, nitrate), lipid-lowering therapy (statin), extended-release niacin or fibrates (for low HDL) and exercise.

Multivessel Disease

The application of PCI in patients with multivessel disease remains controversial, particularly in the setting of diabetes mellitus. Multiple randomised trials have compared PCI with bare metal stents to coronary artery bypass graft surgery (CABG) in selected patients with multivessel coronary artery disease, and rates of survival free from myocardial infarction have been similar. Typically, patients treated with PCI require more subsequent revascularisation procedures due to restenosis or incomplete revascularisation. The need to compare the use of DES and CABG in this setting is eagerly awaited.

One-year follow-up data from the much anticipated Synergy Between PCI With Taxus and Cardiac Surgery (SYNTAX) trial was recently announced. 1800 patients were randomised to either CABG or PCI with the Taxus DES5. By 12-month, DES was statistically inferior to CABD for the primary composite end-points of all-cause death, cerebrovasular event, MI and repeat revascularisation (12.1% vs 17.8%, p=0.0015). Indeed, there was no difference between all-cause death and MI between the two groups. However, PCI group had more repeat revascularisation (5.9% vs 13.7%, p<0.0001) due to restenosis or incomplete revascularisation. On the other hand, CABG group has significantly more strokes (2.2% vs 0.6%, p=0.003).

Hence, in view of the hard end points of death or MI, PCI is an appropriate alternative to CABG. However, there is a higher chance of repeated percutaneous procedures if PCI is adopted. On the other hand, there is a higher chance of stroke if the patient is going for CABG. Hence, a detail discussion between the patient, relatives, interventional cardiologist and cardiothoracic surgeon is recommended before making the decision.

Left Main Coronary Artery Stenosis

Significant narrowing of the left main coronary artery has the worst prognosis of any form of coronary artery disease. CABG has been considered standard therapy because restenosis of the left main coronary artery could be fatal. However, with the availability of DES, there is a growth of interest in a percutaneous approach. Indeed, left main coronary artery lesions are routinely treated, for example, in Japan, Korea and Hong Kong.

The MAIN-COMPARE registry study which was carried out in Korea showed there was no significant difference in major outcomes (death, MI or stroke) between PCI with stenting and CABG in patients with left main coronary artery disease6. However, there was a significantly higher rate of target vessel revascularisation in the PCI group.

The MAIN-COMPARE registry study showed that PCI with stenting was safe in left main disease. However, a well-designed and adequately powered prospective randomised trial of the two revascularisation strategies in patients with unprotected left main disease is eagerly needed.

Conclusion

PCI is one of the most frequently performed medical procedures. With the improvement in hardware and accumulation in clinicians' experience, its usage and indications are ever expanding. Patients with unstable angina, non-ST elevation MI, ST elevation MI and moderate to severe angina symptoms should consider PCI as an option of treatment. Their symptoms and prognosis would be improved after the invasive procedure. For those with no or minimal symptoms, they are candidates for PCI if there is objective evidence of significant myocardial ischaemia. Otherwise, medical treatment with aggressive control of cardiovascular risk factors should be considered. In the setting of multivessel disease and left main coronary disease, PCI is a viable alternative to CABG. A higher repeated revascularisation rate, however, is expected.

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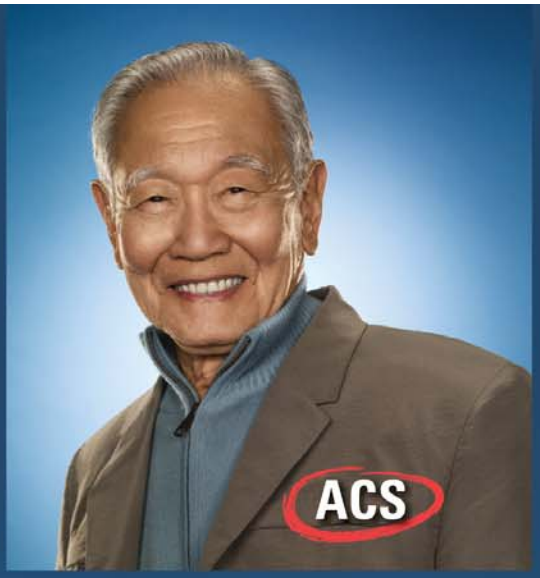

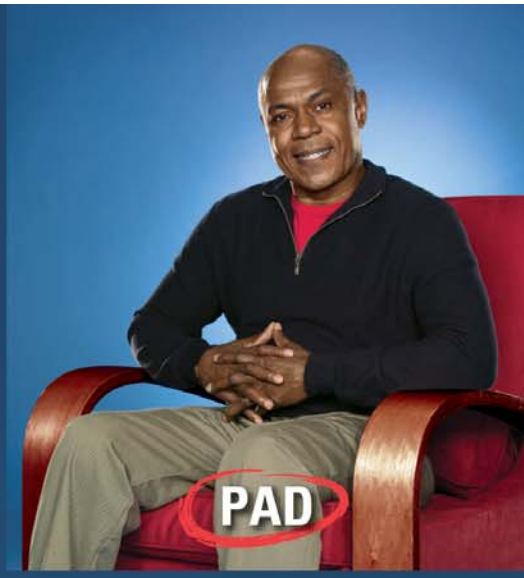

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Electrical Device-Based Therapies for Heart Failure

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Despite advances in pharmacological treatment for heart failure, there are still a growing number of patients with advanced symptoms who suffer from significant morbidity and mortality. This has given rise to the development of device-based therapies which have favourably impacted on the outcomes in patients with heart failure.

Cardiac Resynchronisation Therapy (CRT)

Approximately one third of patients with systolic heart failure have a QRS duration greater than 120 ms, which is most commonly seen as left bundle-branch block. Widened QRS complex represents both inter- and intra-ventricular conduction delays or electromechanical dyssynchrony. Such asynchronous contraction pattern contributes to mitral regurgitation, reduction in stroke volume and subsequently leading to deleterious left ventricular remodelling. CRT delivers electrical stimuli to the left and right ventricles simultaneously with the goal of synchronising the activation of both ventricles. This is achieved by introducing a specially designed pacing lead into the left ventricle -- usually implanted through an intravenous approach via the coronary sinus and into a lateral cardiac vein -- in addition to placement of standard right-sided leads. The proposed mechanism of benefit by CRT is to correct the dyssynchrony between the right and left ventricles and the intraventricular dyssynchrony within the left ventricle by pacing the right ventricular apex and lateral or posterolateral wall of the left ventricle. Minimising intraventricular dyssynchrony has been shown to increase left ventricular filling time, decrease septal dyskinesis, reduce mitral regurgitation and improve global left ventricular function. These acute mechanical effects are accompanied by more chronic adaptations that lead to long-term benefits including improvements in neurohormonal status and left ventricular ejection fraction (LVEF) and reversing the adverse left ventricular remodelling[1].

CRT alone or combined with implantable cardioverter defibrillator (CRTD) are now standard of care for moderate to severe heart failure patients with cardiac dyssynchrony. Results from randomised, controlled trials have consistently demonstrated significant improvements in quality of life, functional status, and exercise capacity in patients with New York Heart Association (NYHA) Class III and IV heart failure who are assigned to CRT. In these patients, cardiac resynchronisation has also been shown to improve cardiac structure and function while significantly reducing the risk of worsening heart failure. Survival benefit by CRT has also been demonstrated in COMPANION (Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure) and CARE-HF (Cardiac Resynchronization-Heart Failure) trials. In COMPANION, CRT pacing with or without ICD capability was associated with a significant one-year relative-risk reduction of about 20% for all-cause death or hospitalisation when added to optimal medical therapy in over 1600 patients with ischaemic or nonischaemic NYHA class III to IV heart failure, an LVEF <35%, and a QRS interval of >120 ms[2]. CARE-HF randomised 813 patients with NYHA class III to IV heart failure despite standard drug therapy, an LVEF <35%, and QRS duration of at least 120 ms. Those with a QRS duration of less than 150 ms were required to have echocardiographic confirmation of ventricular dyssynchrony. Over a mean follow-up of nearly 30 months, CRT was associated with significant 37% reductions in the risk of the primary end point (all-cause mortality or an unplanned cardiovascular hospitalisation). There was a 36% relative reduction in all cause mortality and a 10% reduction in absolute risk in addition to standard pharmacologic therapy[3]. Based on the results from these large-scale randomised trials, the heart failure management guidelines of the American Heart Association (AHA) and American College of Cardiology (ACC) have incorporated CRT as a Class I indication for patients with ejection fraction less than or equal to 35%, NYHA Class III or ambulatory Class IV, sinus rhythm and QRS duration greater than or equal to 120ms despite optimal heart failure medication[4]. Recently, the indication of CRT has been extended to patients with chronic atrial fibrillation or continuous right ventricular pacing. For Class III or ambulatory Class IV patients with cardiac dyssynchrony who have atrial fibrillation or who have frequent dependence on ventricular pacing, CRT is also a reasonable treatment option (Class IIa indication) according to the 2008 ACC/AHA Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities[5]. Preliminary data have suggested that CRT may also be beneficial in patients with less symptomatic heart failure and in patients with normal QRS complex but with evidence of other parameters of cardiac dyssynchrony. Further data are required before extending the device indications beyond those currently authorised by the guidelines.

With advances in technology, the delivery of left ventricular lead is much easier than those of early generation though the procedure is still not risk-free.

Complications, though uncommon, related to positioning of the left ventricular lead include coronary sinus dissection or perforation, lead dislodgement, diaphragmatic pacing and contrast nephropathy. The overall success rate for CRT implantation ranges between 85 to 95%. However, a significant proportion of eligible patients after successful implant do not respond to CRT, the so-called non-responders. The non-response rate is up to around 30% in terms of clinical improvement. Potential causes for poor response to CRT include inappropriate patient selection, suboptimal left ventricular lead implantation site, left ventricular scarring and inappropriate programming of the atrioventricular and interventricular intervals after the procedure[6].

Implantable Cardioverter Defibrillator (ICD)

The implantable cardioverter defibrillator (ICD) is the single most effective treatment for the prevention of sudden cardiac death in patients at risk or who have had resuscitated sudden cardiac death. There is no argument that ICD should be used for secondary prevention once heart failure patients have resuscitated cardiac arrest or documented haemodynamically significant ventricular tachycardia. The role of ICD has now been extended for primary prevention of sudden cardiac death in heart failure patients who have poor left ventricular function.

Patients with heart failure are at risk of sudden cardiac death. Heart failure is a major cause of sudden cardiac death and more than half of the deaths of patients with heart failure are due to sudden cardiac death. The Sudden Cardiac Death in Heart Failure (SCD-HeFT) study addressed the prophylactic effectiveness of ICD devices in decreasing mortality in patients with heart failure of either ischaemic or nonischaemic aetiology and an LVEF <35% and without ventricular arrhythmias[7]. In SCD-HeFT, ICD therapy was more effective than pharmacological therapy in preventing mortality among patients with mild to moderate heart failure. The study showed that ICD therapy was associated with a decreased risk of death of 23% after five years of therapy. This mortality benefit was observed in patients who were already optimally managed on drug therapy. In the latest ACC/AHA/HRS 2008 Guidelines for Device Based Therapy of Cardiac Rhythm Abnormalities[5], ICD therapy is indicated (Class I, Level of evidence: A) in all symptomatic heart failure patients in NYHA functional Class II or III when the LVEF is < 35% due to previous myocardial infarction who are at least 40 days post infarct. Similarly, ICD therapy is also indicated in patients with nonischaemic dilated cardiomyopathy who have an LVEF less than or equal to 35% and who are in NYHA functional Class II or III[8,9]. (Class I, Level of Evidence: B). Since ICD is an expansive device, these recommendations should be applied only to patients who are receiving optimal medical therapy and have a reasonable expectation of survival with good functional status for more than 1 year.

Cardiac Contractility Modulation (CCM)

Only a proportion of heart failure patients can benefit from CRT, because it is only applicable to patients with evidence of cardiac dyssynchrony and as many as 30% of implanted patients are considered non-responders. A new form of electrical therapy, called cardiac contractility modulation (CCM), has been proposed for enhancing ventricular contractile strength independent of the synchrony of myocardial contraction. This technique involves implanting a pacing-type device, with a sensing lead in the right atrium and two right ventricular leads that deliver relatively large amplitude electrical stimuli during the absolute refractory period of the myocardium. The mechanism of effect is thought to be due to improved cardiac myocyte calcium handling without increasing myocardial oxygen demand. Preliminary studies have shown that CCM therapy can enhance contractile performance acutely, reverse remodelling as evidenced by reduction of left ventricular systolic volume and reverse the cardiac mal-adaptative myocardial foetal gene expression[10]. A randomised, double blind, cross-over study showed that after three months of CCM therapy in 164 patients with LVEF of less than 35% and in NYHA Class II to III, exercise tolerance in terms of peak oxygen consumption and quality of life score significantly improved[11]. CCM is a potential device therapy for heart failure patients who are not CRT candidates. Larger scale studies of CCM therapy are underway to confirm its benefit. CCM therapy is now available for commercial use in Hong Kong.

Conclusion

With the advances of device-based therapies and optimal pharmacological treatments, the outcomes of patients with heart failure have much improved. However, many heart failure patients are not receiving the appropriate therapies recommended by treatment guidelines. Recent studies showed that only around 40% of patients eligible for CRT or ICD received them [12]. There are deficiencies in heart failure care, particularly when it comes to device-based therapies, which are more complicated for physicians to deal with than are drug therapies. Understanding the effectiveness and latest indications of these device-based therapies can help us to select patients who will benefit from these treatments.

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Dermatological Quiz

Dermatological Quiz

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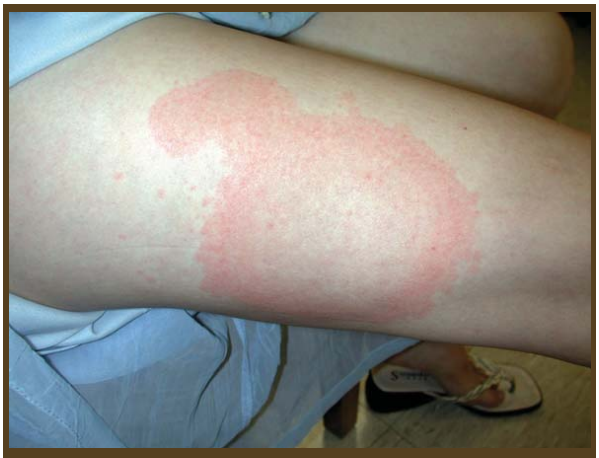

Fig 1: Annular erythematous eruption at right thigh

A 30-year-old woman complained of non-pruritic skin lesions over her thighs and abdomen. The individual lesion spread rapidly to a large size within 1-2 weeks (Figure 1). There were no associated systemic symptoms. Her past health was good. On physical examination, there were figurate erythematous lesions over thighs and abdomen. The lesion at right thigh was annular with elevated edge and central clearing. There was absence of scaling.

Questions:

1. What is your preliminary diagnosis and what are the four classic figurate erythemas?
2. How do you reach the diagnosis in this lady?
3. What investigations will you perform?
4. What will be your treatments?

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- Significant improvements in parameters of metabolic syndrome, including HDL-C and triglyceride levels.[4,5]

Delay of Atherosclerosis

- Slowed the progression of carotid intima-media thickness – predictor for heart attack and stroke.[4]
- Lowered the rate of progression of coronary atherosclerosis significantly as shown by reduction in PAV (percent atheroma volume) of coronary arteries in patients with coronary disease and type 2 diabetes.[6]

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27.8% Risk reduction in non-fatal stroke in elderly patients (p=0.04)[3,*]

18% RRR in incidence of retinopathy in type-1 diabetes (p=0.051)[4,*] New**

34% Increase in regression of retinopathy in type-2 diabetes (p=0.009)[5,*] New**

CHF: Chronic heart failure; **RRR:** Relative risk reduction.

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Atrial Fibrillation Catheter Ablation

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Specialist in Cardiology

Dr. Yui-chi So

Introduction

In China Mainland, a cross -sectional survey of AF conducted from 2005 to 2006 including 19,368 participants (8,636 men, 10732 women) aged >= 35 years showed that the prevalence of AF in Chinese adults was 0.73% (0.74 % in men and 0.72 % in women). The AF incidence was 0.43% in men and 0.44 % in women with age <60 years old, and was 1.83 % in men and 1.92 % in women for age >= 60 years old. AF prevalence was estimated to be 0.41 % around 5.3 million patients in the Mainland.

In the United States, AF prevalence was estimated to be 2.3 million. Between 1980 and 1999, AF hospitalisations increased 80 % for patients aged 45-65 and doubled for patients 65 yrs or older. The ageing of the population alone is expected to raise the number of AF from 2 million in 1995 to more than 3 million by 2020 and 5.6 million by 2050.

Framingham data showed that at age 40, there is a risk of 1/4 to develop AF. 1.3 % of individuals in the elderly population in Hong Kong had AF.

Paroxysmal AF

Defined as an AF episode which spontaneously terminates within 7 days.

Persistent AF

Defined as an AF episode which lasts for more than 7 days or requires cardioversion.

Permanet AF

An AF episode which fails to terminate with cardioversion or terminates and relapses within 24 hours.

Epidemiology

In China, the percentage of AF of first diagnosed were 30.9 %; paroxysmal 33 %, persistent 7.2 % and permanent 28.9 % respectively.

The recurrence rate of AF is around 49-90 %. In the Stroke Prevention trial, the independent predictors of recurrence were left atrial enlargement and a history of myocardial infarction. Around 18-33 % of patients will develop permanent AF. Old age and AF at presentation predicted transition to permanent AF.

However, many PAF episodes are asymptomatic. A transtelephonic ECG monitor found that asymptomatic PAF was 12 x more frequent than symptomatic ones.

Aetiologies

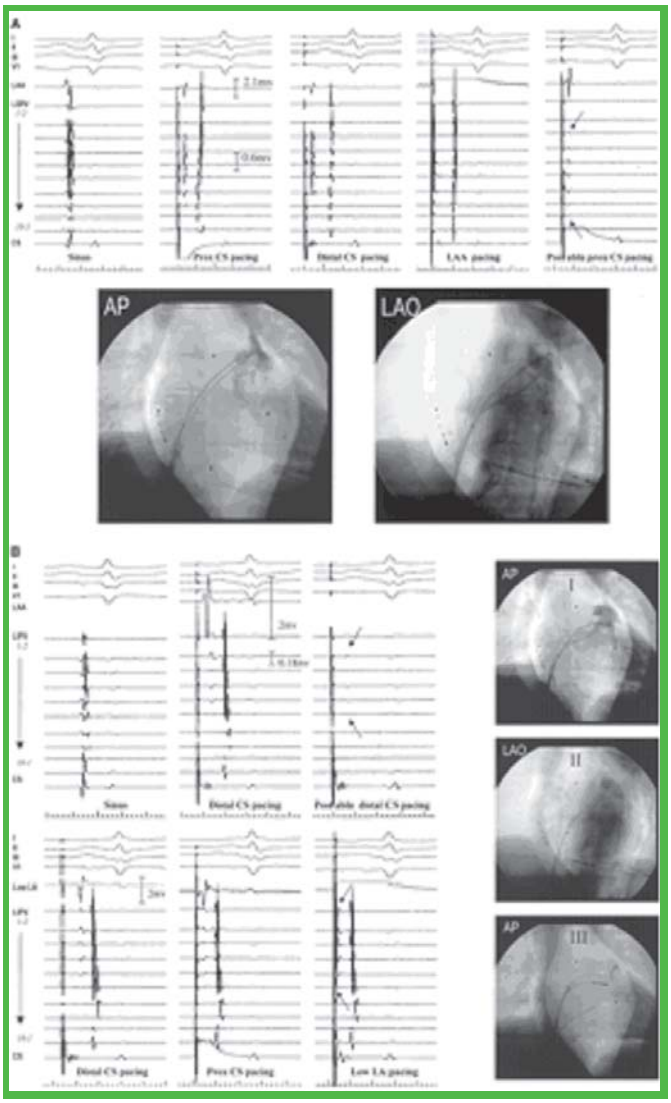
1. Idiopathic (lone AF)
2. Increased LA pressure
3. Ischaemia
4. Inflammatory
5. Age related (fibrosis and amyloid)
6. Alcohol
7. Increased sympathetic activity such as thyrotoxicosis, anxiety, exercise
8. Increased parasympathetic activity such as during sleep
9. Congenital heart disease such as ASD
10. Neurogenic such as Subarachnoid haemorrhage
11. Familial
12. Sick sinus syndrome

Foci of AF

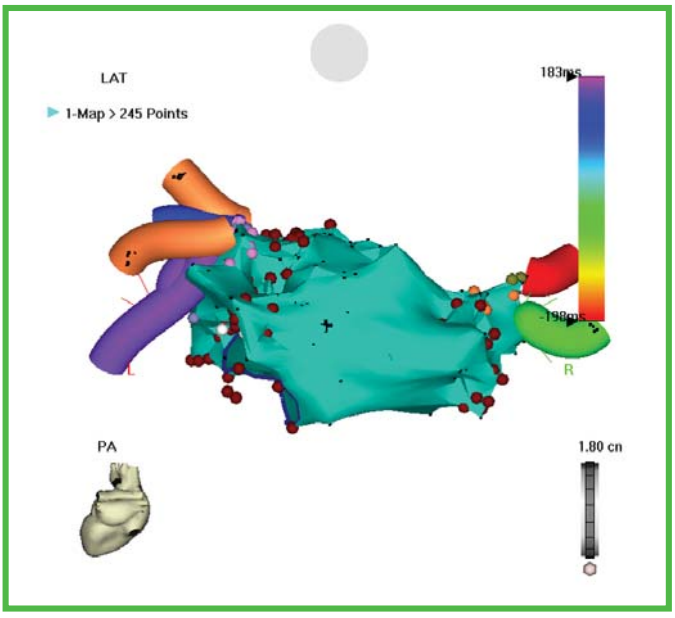
a) Pulmonary vein(PV) ectopic beat for AF initiation:
There are myocardial sleeves in the embryonic development of pulmonary veins which give rise to abnormal automaticity. Many evidences show that there is dilation of PV ostia in patients with AF. These demonstrate that haemodynamic factors and stretch mechanisms may account for PV ectopic beats. Haissaguerre first studied the mechanism of spontaneous onset of AF was due to PV ectopic triggers. Investigators also demonstrated that PV activity may also have a role in maintaining AF too.

PV ablation

1. Focal ablation- The PV potential which initiates AF had high frequency spikes. Therefore, it is logical to directly ablate the PV potential. However, the recurrence rate is high even after ablating the PV potential at OT site. Moreover, it will cause PV stenosis. Inconsistent inducibility, multiple and new foci of triggers are among the failure reasons for AF initiation.



2. Segmental ablation- There is an extension of left atrium muscle to the PV. Therefore, ablation at the ostium of PV using a Lasso catheter can easily identify the breakthrough sites from left atrium (LA) to PV. Pappone using the Carto system (3D mapping system) applied circumferential ablation of PV orifice. He reported that there was more than 80 % successful rate.



3. Linear ablation- The left atrial wall especially the left posterior left atrium is involved in the initiation and maintenance of AF. Therefore, ablation of the left atrial wall, PV ostial atrial tissues and mitral annulus atrial tissues are necessary in treating chronic AF. The noninducibility of AF as end point for linear ablation in Bordeaux group increased the successful rate of AF ablation.

b) Other Thoracic Foci of AF

SA node derives from sinus venosus embryologically. However, there are other areas of thoracic veins which are also remnants of sinus venosus such as SVC, coronary sinus, etc.

1. **Superior vena cava (SVC)** - The junction between SVC and right atrium contains myocytes that has pacemaker activity. If there is enhanced automaticity this will play as a trigger for AF. Clinical study confirmed that there is a layer of myocardial tissue on the dorsal surface of SVC
2. **Coronary sinus (CS)** - In animal studies, there is automatic rhythmic activity triggered by catecholamines. Clincially, we prove that there are a lot of fractionated potentials in CS.
3. **Crista Terminalis** - Hogan found that there are atrial fibres all along the border of crista terminalis which has spontaneous discharge. This may also account for initiation of AF.
4. **Ligament of Marshall**- It is the embryonic sinus venosus and left cardinal vein running between the superior and inferior left pulmonary veins. It is found that there is atrial musculature which runs in from coronary sinus. This musculature has also been found to have triggered activity.
5. **Left sided posterior atrial wall**- For diseased atria, the musculature is hypopolarised and can produce ectopics which may trigger AF. The mechanism may be slow depolarisation of phase 4 or delayed after depolarisation triggers after isoprenalin.

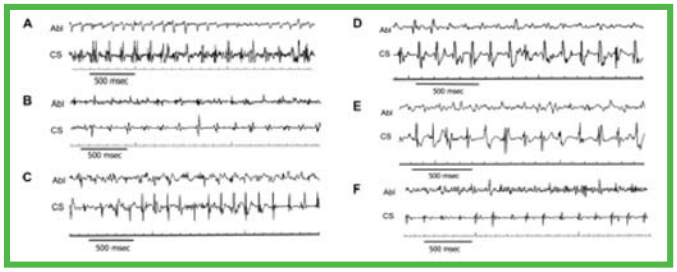
Non- PV ectopics account for around 25% of patients who have recurrences of AF. 15-25 % of patients actually have non-PV triggers.

Complex Fractionated Atrial Electrograms CFAE

Another approach of ablating AF suggested by Professor Nademanee is to ablate the Complex Fractionated atrial electrograms (CFAE):

Defined : 2 deflections or more with fluctuating baseline or atrial electrograms with a very short cycle length (< 120 msec).

It was thought that by ablating the CFAE, the ganglionic plexi (GP) will be modified. Therefore , the maintenance substrate of AF was also modified too.



Post Ablation Management

We start anticoagulation after 4 hours of sheath removal. Nowadays we usually use the LMWH. Oral warfarin is also started at the same time. We anticoagulate the patient for around 30 days. Anticoagulation will be stopped after 3 months treatment if there is no more AF recurrence. Anti-arrhythmic drugs are also prescribed for 1-3 months.

Breakthrough attacks of AF and atrial tachyarrhythmia are quite common within the 1st month. Therefore, we can only label success or not after at least 1 month's time.

Complications

Pericardial effusion 0.1%
Stroke 0.03%
TIA 0.2 %
Cardiac tamponade 0.1%
Severe PV stenosis 1%
Phrenic nerve palsy 0.5 %
atrio- oesophageal fistula 0.05%
atrial flutter or tachyarrhythmia 5-10 %
Death <0.1%

Successful Rate of AF Ablation

Nowaday, we use different approaches of AF ablation and we can report the successful rate at around 80%-90% for 1 year. It also depends on the age of the patient (>70 yrs old); underlying heart disease etc.

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Acertil is a long-acting ACE inhibitor. **International nonproprietary name:** Perindopril. **Indications:** Essential hypertension. Congestive heart failure (adjunctive therapy). **Dosage and administration:** Hypertension: 4mg once a day in the morning. If necessary, the dose may be increased to 8mg after 1 month of treatment. Acertil should be taken before food. Congestive heart failure: Acertil should be started under close medical supervision at a starting dose of 2mg in the morning. This may be increased to 4mg once blood pressure acceptability has been demonstrated. Elderly patients: start treatment at 2mg daily. **Contraindications:** Children. Pregnancy. Lactation. Patients with a history of hypersensitivity to Acertil. **Precautions:** Assess renal function before and during treatment where appropriate. Renovascular hypertension. Surgery/anesthesia. Renal failure: the dose should be cautiously adjusted in accordance with the creatinine clearance (refer to complete data sheet). Symptomatic hypotension is rarely seen, but is more likely in volume-depleted patients, those receiving diuretics, or with the first two doses. In diuretic-treated patients, stop the diuretic 3 days before starting Acertil. A diuretic may later be given in combination if necessary; potassium-sparing diuretics are not recommended. Combination with neuroleptics or imipramine-type drugs may increase the hypotensive effect. Serum lithium concentrations may rise during lithium therapy. **Side effects:** Rare and mild, usually at the start of treatment. Cough, fatigue, asthenia, headache, disturbances of mood and/or sleep have been reported. Less often, taste impairment, epigastric discomfort, nausea, abdominal pain, and rash. Reversible increases in blood urea and creatinine may be observed. Proteinuria has occurred in some patients. Rarely, angioneurotic edema and decreases in hemoglobin, red cells, and platelets have been reported. **Composition:** Each tablet contains 4mg of the *tert*-butylamine salt of perindopril. **Presentation**: Packs of 30 tablets of Acertil 4mg (scored) . ***As prescribing information may vary from country to country, please refer to the complete data sheet supplied in your country.*** **Les Laboratoires Servier -** France. Correspondent: **Servier International,** 22, rue Garnier, 92200 Neuilly-sur-Seine, France.

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Lipid Control for Heart Disease

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Dr. Tsan-fai Chan

Coronary artery disease is the largest cause of premature death in industrialised nations and is a growing threat in developing countries as well. The central role of cholesterol in the pathophysiology of coronary artery disease leads to lipid-lowering therapy for the medical management of this condition.

Clinical research with trials using statins have demonstrated the benefits of serum cholesterol lowering in cardiovascular outcome of our population, ranging from healthy subjects to patients with overt cardiovascular risk and patients suffering from acute coronary syndrome. Our threshold of serum cholesterol lowering has been decreased as compared with the past, especially for patients with higher cardiovascular risk. Below will be a review of some of the trials that can help us to look into the extent of cholesterol lowering that will be beneficial to our patients.

In the Heart Protection study[1], patients with a history of coronary artery disease and low-to-average total or LDL cholesterol (LDL-C) levels, persons at risk for coronary artery disease due to a history of other vascular disease (peripheral vascular disease or stroke); those who had a history of diabetes, and individuals who had been inadequately studied in the past (patients > 70 years of age, females) are studied. Between July 1994 and April 1997, 20,536 individuals were assigned to simvastatin (40 mg/day), against placebo tablets, or to a cocktail of antioxidant vitamins (600 mg vitamin E, 250 mg vitamin C, and 20 mg beta-carotene) against placebo capsules, for a mean duration of at least 5 years. It was shown that subjects with LDL-C < 2.56mmol/L did benefit from further LDL-C level lowering and the risk of cardiovascular events decreased significantly in all subgroups, irrespective of baseline LDL-C

The Asian population, a group that has been traditionally considered to be at much lower risk than Western counterparts; will we benefit from primary prevention with cholesterol lowering? The management of elevated cholesterol in the primary prevention of adult Japanese (MEGA) trial[2] was the first large randomised trial of statins therapy in an Asian Population. The aim of the MEGA study was to evaluate the effect of cholesterol reduction with pravastatin on the incidence of cardiovascular disease in subjects with mildly elevated total cholesterol and no evidence of atherosclerotic disease and to evaluate the long-term safety of pravastatin in Japanese patients. A total of 8214 patients were randomised to diet or diet plus pravastatin 10-20 mg/day. All patients were advised to follow the National Cholesterol Education Program (NCEP) step 1 diet, which is low in cholesterol and saturated fats. The primary endpoint of the trial, the first occurrence of the CHD endpoint (fatal and nonfatal myocardial infarction [MI], angina, cardiac or sudden death, or cardiac or vascular intervention) was significantly reduced by 33% in the pravastatin group compared with the diet-alone group ($P < .010$) The effect of pravastatin on the primary endpoint was observed early, and reached significance at 4 years. Patients having higher risks will have more benefits, including subgroups such as man > 60 years of age and baseline LDL > 4.01 mmol/L.

Coronary intervention has an important role in the treatment of ischaemic heart disease, especially for patients suffering from acute coronary syndrome or acute myocardial infarction. However statins therapy is also very important as part of the medical management of this group of patients.

In the PROVE IT-TIMI 22 study[3], 4162 patients with an acute coronary syndrome (ACS) within the preceding 10 days were randomly assigned in a 1:1 fashion to pravastatin 40 mg or atorvastatin 80 mg daily. All patients had a total cholesterol level ≤ 6.21 mmol/L but patients who were receiving long-term lipid-lowering therapy at the time of their index ACS had to have a total cholesterol level≤5.18 mmol/L .The primary end-point was a composite of death from any cause, myocardial infarction, documented unstable angina requiring re-hospitalisation, revascularisation (performed at least 30 days after randomisation) and stroke. The median LDL-C achieved during treatment 2.46 mmol/L in the standard therapy group and 1.60 mmol/L in the high-dose group ($p < 0.001$). Primary end-point at 2 years was 26.3% for standard therapy and 22.4% for intensive therapy, showing the benefit of intensive therapy ($p = 0.005$; 95% CI: 0.74-0.95). Muscle-related side effects were low and not significantly different between groups. There were no cases of rhabdomyolysis.

The Treat to New Targets/treat to new targets (TNT)[4] has compared standard dose (10mg) and high dose (80mg) of atorvastatin in patients with stable coronary artery disease. It has shown that LDL-C lowering down to 2 mmol /L has further risk reduction compared with a LDL level of 2.6 mmol /L in the primary endpoint of coronary heart disease death, myocardial infarction, resuscitated cardiac arrest and stroke.

Role of Trans Fatty Acids

Consumption of dietary Trans fatty acids is associated with a deleterious increase in small, dense low-density lipoprotein (LDL) cholesterol particles. Dietary Trans fatty acids are formed during the process of hydrogenating vegetable oil and should be reduced in our dietary component.

Beyond LDL-C Reduction

The main atheroprotective mechanism of HDL is related to its ability to facilitate the reverse cholesterol transport pathway, by which excess cholesterol from peripheral cells, such as macrophages, in the vessel wall is transported to the liver for excretion. HDL has been shown to prevent endothelial dysfunction; it inhibits the expression of adhesion proteins by endothelial cells, which mediate the initial attachment and infiltration of monocytes into early plaques. HDL also has favourable effects on the vasomotor tone of vessels, by promoting the nitric oxide production of endothelial cells, which increases vasodilatation and suppresses smooth muscle cell proliferation in plaques. HDL reduces platelet activation and promotes fibrinolysis and thus may inhibit the formation of a thrombus over ruptured plaques. A combined approach of simultaneously lowering LDL-C and raising HDL may be more effective in reducing cardiovascular events than only lowering LDL-C.

Other than pharmacological therapy, exercise is useful for increasing the HDL level. Currently, the most effective drug for increasing HDL is niacin but its use has been limited because of side effects. Cholesteryl ester transfer protein inhibitors are effective to elevate HDL but in the Investigation of lipid Level management to understand its impact in atherosclerotic events trial (ILLUMINATE) has demonstrated its negative effect. The trial is terminated early because it had recorded 82 deaths in the patients taking torcetrapib-atorvastatin against 51 in patients taking atorvastatin alone. In addition to the increase in mortality, the rates of myocardial infarction (MI), revascularisation, angina, and heart failure were higher in the torcetrapib-atorvastatin arm.

Other HDL Replacement Therapy

Apo-lipoprotein A-I is one of the protein components of HDL and is a natural choice for therapeutic HDL replacement. APOA-IMilano (ETC-216), a synthetic Apo-lipoprotein AI has been developed as a therapeutic agent for HDL replacement. The first clinical study of the effect of ETC-216 in humans was assessed by intravascular ultrasound on patients with acute coronary syndrome.[5] In this trial, 57 patients were given weekly infusions of ETC-216 at 15 and 45 mg/kg or placebo for 5 weeks and were assessed by intravascular ultrasound at baseline and after the 5-week treatment period. The average decrease in plaque volume for the ETC-216 treatment group was 4.2% compared with baseline, whereas there was a slight increase in plaque volume of 0.14% in the placebo group, which was statistically significantly different from the treatment group. Other secondary measures, such as absolute change in plaque volume and maximum atheroma thickness, also showed a favourable statistically significant improvement. Based on the analysis of the position of the external elastic membrane, atheroma volume in the most diseased segments was reduced by 10.9% on average after treatment with ETC-216. However HDL replacement is still not available for our daily management of patients.

In summary among those at risk of cardiovascular disease, lipid lowering with statins confers similar cardiovascular risk reduction across all ranges of baseline LDL-C and clinical benefit is related to the absolute reduction in LDL-C. Level of < 2.0 mmol/L should be the target in patients having cardiovascular risk. Exercise as a means for HDL raising should be advocated to our patients.

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宋代名瓷簡介

葉承標醫生

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英國愛丁堡皇家內科醫學院榮授院士, 香港醫學專科學院院士(內科)

葉承標醫生

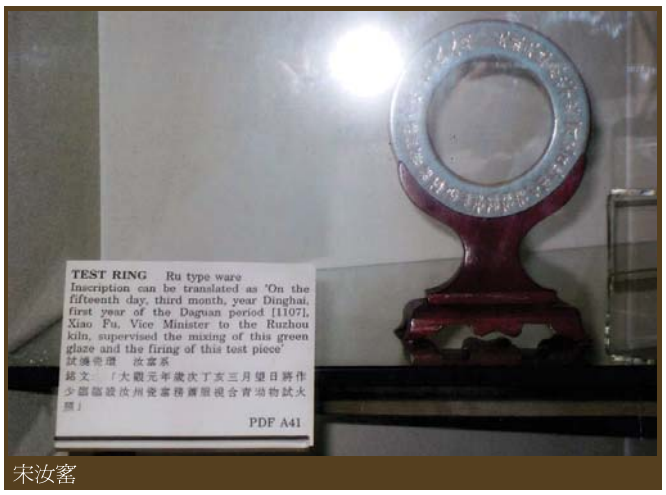
中國瓷器之發展始於商代，當時之原始青瓷經歷數百年之演變及改良，至周、秦、漢、南北朝之青瓷已甚爲可觀，更有多彩瓷器之首次出現。唐代之瓷器更有長足之發展，如邢窯白瓷，長沙窯，越窯包括秘色瓷更是中國瓷藝之極品。秘色瓷其中一重要影響是它可以看作是‘官窯’的前奏，因爲它是貢品；而宋代之前是沒有官窯概念的。

無可否認宋代爲中國瓷藝發展之一高峯，其一原因是當時重文輕武，文學及藝術創意無限，不同瓷器品種百花齊放，南北爭輝。隨了名聞中外之五大名窯 ： 汝，官、哥、定、鈞 之外，此外耀州、龍泉、影青、建窯等也是很傑出之窯系，對後世之瓷器發展有深遠之影響，爲歷代收藏家的喜愛：乾隆皇帝曾在宋五大窯之精品上提詩文，亦有下旨令仿製宋之五大名窯，可見其喜愛宋瓷之程度。宋瓷因爲年代較明、清代的瓷器爲早，故數量亦相對地較少：如台北故宮博物館有宋、元瓷器一千五百件左古，但明、清瓷則有一萬多件，其數量之差別相當大。宋瓷之官窯、哥窯在國際拍賣會上常放異彩，而官鈞瓷之價格亦有節節向上的趨勢；三、四十年前宋瓷的價值常比明、清瓷爲高，只是在近二十年左右才被後者趕上，但看來這程景大有可能在不久之將來有所逆轉。

然而現今之所公認之五大各窯爲 ： 汝、官、哥、定、鈞 實乃明朝後期/清朝早期之後之共識。明代文獻列出柴、汝、官、哥、定爲宋之五大名窯。相傳柴窯乃五代後周世宗柴榮所指示制作之御窯：釉色是‘雨過天青雲破處，這般顏色作將來’。天青大概是淺藍或淡青色；現今所知道的品種有類似的可能是影青湖田窑、耀州、鈞窯、越窯等。但由於柴世宗在位只是六、七年左右，他所指示的工匠不知能否按他的批示完成使命，柴窯的窑址至今仍未被發現，而且至今亦沒有一件標準的傳世器，明代的文獻已經表明柴窯已很難找到了，所以有些專家甚至認爲柴窑並不全在，或未曾有規模地生產過。到了清代柴窯便被鈞窯所取代，而形成現今之宋代五大名窑爲‘汝、官、哥、定、鈞’。

汝窯

汝窯爲五大名窯中排行第一：南宋文獻‘汝窯爲魁’，絕不是浪得虛名！汝窯是北宋早期時代替定窯而燒製的御瓷，時間只有二十年左右，傳世只有約一百件；絕大部份收藏在大博物館如台北故宮博物館、北京故宮博物館、上海博物館、英國大維德基金(Percival David Foundation)及倫敦大英博物館。每一件都是國寶級文物。窯址已在二十多年前發現在河南省寶豐清涼寺。汝窯的特徵是香灰胎、魚鱗狀開片、底部有細小的芝蔴釘。釉色以天青爲主，汝窯釉有瑪瑙末作爲原料，器物一般形制不大：如碗、盞托、碟、瓶、洗、樽等。汝瓷清雅脫俗，其他品種之瓷器都相形見拙。



宋汝窯

官窯

北宋時很有可能已有御製之官窯，雖然窯址並未發現，但專家認爲宋徽宗時可能已燒製官窯，窯址可能在宋代的汴京附近，但因被黃河之水淹沒已被深深埋在地下，故窯址很難找到。根據傳世品北宋官窯多有紫口鐵足之特徵，與南宋之官窯不一樣，南宋官窯的窯址已在老虎洞、烏龜山等地方被發現，釉色則主要有天青、粉青或月白等色。釉面常有開片狀及呈乳濁感，形態簡樸，莊飾不多，爲中外收藏家所喜愛。宋官窯瓷器在拍賣場上罕有地亦會亮相。


宋官窯

定窯

定窑是由唐朝之邢窯發展之著名白瓷，始燒於晚唐，宋、金代極其繁盛，影響甚爲深遠，其後更成爲北方之一大窯系。除了最常見的白瓷之外，還有黑定、紫定等。中心窯場在河北省曲陽縣。定窯造形清雅精緻：有印花、刻花爲常見，常見的品種有碗、盤、碟、瓶、罐等。釉面之出現淚痕是它的特徵。宋代白瓷甚多，但定窯是名窯，其一般價值會比普通其它的白瓷高。其中刻花梅瓶 (Percival David Foundation,UK) 和孩兒枕 (北京故宮博物館)皆是精品。北宋被金滅後，北方定窯工場受到破壞，工匠紛紛逃到南方，在景德鎮繼續燒製和定窯非常相似的製品，稱爲 ‘ 南定 ’ 。

哥窯

哥窯也是一個充滿疑問的窯場，它之生產時間大有爭議。它的型制有些和官窯類似，甚至難於分辨。宋代文獻沒有哥窯的記載，它的名稱始見於元代，而明初宣德年間，被列爲名窯之一。其形制則常常模仿古代青銅器：如貫耳壺、盤、爐、瓶等。如果習中欣賞它的藝術水平則確是自成一格，無與倫比。它的特徵是器物滿佈開片，其中有鐵黑色的大釉裂紋 和金黃色的小釉裂紋，或有‘金絲鐵線’之稱，其他特徵包括深的胎色‘紫口鐵足’，釉色主要是灰青色或米黃包。大部份的藏品也是在各大博物館。近數年在拍賣場上也偶爾會碰到哥窯瓷，後世仿哥窯的瓷器非常多。

宋哥窯

鈞窯

鈞瓷最吸引收藏家、觀賞家的就是它的釉色了。它主要是不用深淺的藍色來展示它的美感和藝術 ： 有月白、天青、天藍色。釉的厚薄不一，是鑑定真品及仿品之一重點。釉的其他重要特徵還有蚯蚓走泥紋及細小的’棕眼’。 因爲燒製時要控製温度左當時的環境有一定的困難，而燒製時温度不夠 (少於 1350 C) 則釉色偏暗，要掌握準確之窯温度常常失敗，故鈞窯有十燒九不成及重釉不重胎之稱。宋瓷以清雅稱著，鈞瓷是典形的表表者。常見的形制有碗、碟、爐、瓶類比較少見。有一系列的種類是屬於官廷用品：如花盆、水仙盆、渣斗等，稱爲官鈞，明顯與一般民間用的品種不一樣，而燒製年份亦有爭議：有北宋、金、元或早明的說法，直到目前還未有定論。鈞瓷發展到元代時器形較大，釉上常有紫紅斑作爲裝飾(釉加了銅元素)或添上雙直耳、貼花等裝飾。雖未及宋鈞那麼優雅，但仍具有相當的可觀性。因爲鈞瓷那麼吸引，所以明、清代有不同的仿鈞窯出現：如爐鈞、石灣鈞等，可見鈞窑對後世瓷器的影響。

宋鈞窯

Federation President Cup Soccer Five Tournament 2008

After rounds of exciting matches, the President Cup Soccer Five Tournament 2008 came to an end on 30th November 2008 at Ying Wa College. Congratulations to Janssen Pharmaceutica, Pfizer Corporation Hong Kong Ltd and Hong Kong Occupational Therapy Association for being the winners of this year.

Champion - Janssen Pharmaceutica

1st Runner up - Pfizer Corporation Hong Kong Ltd

2nd Runner up - Hong Kong Occupational Therapy Association

Dr. Amy Pang's Photography Talk

On the 25th November, the Federation invited Dr. Amy Pang to host a photography talk to members of the medical profession. Dr. Pang shared with the audience photos taken during her numerous travelling photographic expeditions, including China, Europe and Africa. Every picture tells a story. Rather than just explaining the technical perspective, Dr. Pang also told the interesting and exciting experience behind each picture. It was an informative and entertaining talk that fascinated the audience for the whole evening.

Executive Committee Members for 2008-2009

We are pleased to announce the new Executive Committee members for 2008-2009 of the Federation of Medical Societies of Hong Kong elected at the 23rd Annual General Meeting held on 20th November 2008 as follows:

President:	Dr. FONG To Sang, Dawson
1st Vice President:	Dr. LO See Kit, Raymond
2nd Vice President:	Dr. LO Sze Ching, Susanna
Hon. Secretary:	Dr. CHAN Sai Kwing
Hon. Treasurer:	Mr. LAM Lop Chi, Nelson
Deputy Hon. Treasurer:	Mr. LEE Cheung Mei, Benjamin

Executive Committee Members :

Dr. CHAN Chi Fung, Godfrey
Dr. CHAN Chi Kuen
Dr. CHAN Hau Ngai, Kingsley
Dr. CHIM Chor Sang, James
Dr. CHOI Kin
Dr. LEE Kin Man, Philip
Dr. MAN Chi Wai
Dr. MOK Chun On
Dr. MUI, Winnie
Dr. NG Yin Kwok
Dr. YU Chau Leung, Edwin
Dr. YU Kong San

23rd Federation Annual General Meeting, 20th November 2008

Seated from left to right:
Dr. Winnie MUI, Dr. Godfrey CF CHAN, Dr. MAN Chi Wai, Mr. Nelson LC LAM, Dr. Dawson TS FONG (President), Dr. Raymond SK LO, Dr. CHEUNG Tse Ming, Dr. CHAN Sai Kwing, Dr. CHAN Chi Kuen

Back row from left to right:
Ms. Tina WT YAP, Dr. Maureen ML WONG, Mr. Samuel YC CHAN, Dr. PO Yin Chung, Dr. MOK Chun On, Dr. LIU Shao Haei, Dr. Tony KC NG, Dr. KO Chi Fai, Prof. Stephen HY WEI, Mr. James HM MCGOWAN, Mr. Peter YY TO, Dr. Edwin CL YU

Directors of the HKFMS Foundation Limited for 2008-2009

President:	Dr. FONG To Sang, Dawson
1st Vice President:	Dr. LO See Kit, Raymond
2nd Vice President:	Dr. LO Sze Ching, Susanna
Hon. Secretary:	Dr. CHAN Sai Kwing
Hon. Treasurer:	Mr. LAM Lop Chi, Nelson
Directors:	Dr. CHAN Chi Kuen
	Mr. CHAN Yan Chi, Samuel
	Dr. CHIM Chor Sang, James
	Mr. LEE Cheung Mei, Benjamin
	Dr. WONG Mo Lin, Maureen

News from Member Societies:

Hong Kong Museum of Medical Sciences Society
Updated office-bearers for the year 2008-2009 are as follows: President: Dr. TSO Shiu-chiu; Honorary Secretary: Dr. MA Siu-wing; Honorary Treasurer: Dr. KHOO Ui-soon

Hong Kong Society of Medical Genetics
Updated office-bearers for the year 2008-2009 are as follows: President: Dr. LO Fai Man; Honorary Secretary: Dr. POON Miu Kuen, Priscilla; Honorary Treasurer: Mr. CHAN Wing Kwong

The Hong Kong Society of Gastrointestinal Motility
Updated office-bearers for the year 2008-2010 are as follows: President: Dr. LAI Kam-chuen; Honorary Secretary: Dr. CHAN On-on, Annie; Honorary Treasurer: Dr. LEONG In-son

The Hong Kong Society of Rheumatology
Updated office-bearers for the year 2008-2009 are as follows: President: Dr. MOK Chi Chiu; Honorary Secretary: Dr. TAM Lai Shan; Honorary Treasurer: Dr. CHAN Ka Yan, Helen

The FMSHK would like to send its congratulations to the new office-bearers and look forward to working together with their societies.

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
				1	★ Joint Surgical Symposium - Possibilities & Limitations 2	3
4	★ 保健員文憑課程 5	★ FMSHK Officers' Meeting 6	★ HKMA Choir Rehearsal ★ HKMA Orchestra Rehearsal 7	★ HKMA Council Meeting 8	★ HKMA CME - An Update on Development of Liver Transplantation in Asia 9	★ Refresher Course for Health Care Providers 2008/ 2009 - Common Skin Problems in General Practice ★ 2009 Nursing Conference - Building Healthy City 10
★ A One Day Course - "Synopsis: Oral, Inhalation and Intravenous Sedation in Dentistry" ★ HKMA Structured CME Programme at Queen Elizabeth Hospital Year 08/09 (X) - Eye 11	12	★ FMSHK Executive Committee Meeting 13	★ Hong Kong Neurosurgical Society Monthly Academic Meeting - Mild Traumatic Brain Injury & Post-concussion Syndromes ★ HKMA Shatin Doctors Network - Diagnosis and Management of Overactive Bladder ★ HKMA Choir Rehearsal ★ HKMA Orchestra Rehearsal 14	15	16	★ 4th HKMA Sports Night ★ Photo Seminar: Candid Pictures and Artistic Photography 17
★ HKMA Certificate Course on Family Medicine 2009 18	★ Introduction to the Art of Classical Chinese Poetry Writing 19	20	★ HKMA Choir Rehearsal ★ HKMA Orchestra Rehearsal 21	★ HKFMS Foundation Meeting 22	23	24
25	26	27	28	29	30	31

Medical Diary of January

Date / Time	Function	Enquiry / Remarks
2 8:00 am - 9:00 am **FRI**	**Joint Surgical Symposium - Possibilities & Limitations** Organised by: Department of Surgery, The University of Hong Kong & Hong Kong Sanatorium & Hospital Chairman: Dr. Angus C.W. CHAN Speakers : Prof. William I. WEI & Dr. CHAN Yu-Wai # Auditorium, 4/F, Li Shu Pui Block Phase II, Hong Kong Sanatorium & Hospital	Department of Surgery, Hong Kong Sanatorium & Hospital Tel: 2835 8698 Fax: 2892 7511 1 CME Point (Active)
5 **MON**	**保健員文憑課程** Organised by: College of Nursing, Hong Kong	Secretariat Tel: 2572 9255 Fax: 2838 6280
6 8:00 pm - 10:00pm **TUE**	**FMSHK Officers' Meeting** Organised by: The Federation of Medical Societies of Hong Kong # Gallop, 2/F., Hong Kong Jockey Club Club House, Shan Kwong Road, Happy Valley, Hong Kong	Ms. Paulina TANG Tel: 2527 8898 Fax: 2865 0345
7 8:00 pm **WED** *(14, 21)*	**HKMA Choir Rehearsal** Organised by: The Hong Kong Medical Association # CR1, Hong Kong Cultural Centre	Ms. Candy YUEN Tel: 2527 8285
8:00 pm *(14, 21)*	**HKMA Orchestra Rehearsal** Organised by: The Hong Kong Medical Association # Pui Ching Education Centre	Ms. Candy YUEN Tel: 2527 8285
8 8:00 pm **THU**	**HKMA Council Meeting** Organised by: The Hong Kong Medical Association Chairman: Dr. H.H. TSE # HKMA Head Office, 5/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Christine WONG Tel: 2527 8285
9 1:00 pm **FRI**	**HKMA CME - An Update on Development of Liver Transplantation in Asia** Organised by: The Hong Kong Medical Association Speaker: Dr. NG Kwok Chai Kelvin # Yue (Chinese Restaurant), 1/F., City Garden Hotel, 9 City Garden Road, North Point, Hong Kong	Miss Viviane LAM Tel: 2527 8452 1 CME Point
10 2:30 pm **SAT**	**Refresher Course for Health Care Providers 2008/ 2009 - Common Skin Problems in General Practice** Organised by: The Hong Kong Medical Association & Our Lady of Maryknoll Hospital Speaker: Dr. HO King Man # Training Room II, 1/F., OPD Block, Our Lady of Maryknoll Hospital, 118 Shatin Pass Road, Wong Tai Sin, Kowloon, Hong Kong	Ms. Clara TSANG Tel: 2354 2440 2 CME Points
8:30 am - 4:30 pm	**2009 Nursing Conference - Building Healthy City** Organised by: College of Nursing, Hong Kong	Secretariat Tel: 2572 9255 Fax: 2838 6280
11 9:00 am - 5:00 pm **SUN**	**A One Day Course - "Synopsis: Oral, Inhalation and Intravenous Sedation in Dentistry"** Organised by: Hong Kong Society of Paediatric Dentistry Chairman: Prof. Stephen WEI Speaker: Dr. Thomas LENHART, DMD # Lim Por Yen Lecture Theatre, HKAM Jockey Club Building, 99 Wang Chuk Hang Road, Aberdeen, Hong Kong	Ms. Zinnia PANG Tel: 2859 0251 Fax: 2559 3803
1:30 pm	**HKMA Structured CME Programme at Queen Elizabeth Hospital Year 08/09 (X) - Eye** Organised by: The Hong Kong Medical Association and Queen Elizabeth Hospital Speaker: Dr. YUEN Kwok Lai Hunter; Dr. NG Sin Yee Anita and Dr. THAM Chee Yung Clement # Lecture Theatre, G/F., Block M, Queen Elizabeth Hospital, Kowloon	Miss Viviane LAM Tel: 2527 8452 (Registration Fee is required) 3 CME Points
13 8:00 pm - 10:00 pm **TUE**	**FMSHK Executive Committee Meeting** Organised by: The Federation of Medical Societies of Hong Kong # Council Chambers, 4/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Paulina TANG Tel: 2527 8898 Fax: 2865 0345
14 7:30 am **WED**	**Hong Kong Neurosurgical Society Monthly Academic Meeting - Mild Traumatic Brain Injury & Post-concussion Syndromes** Organised by: Hong Kong Neurosurgical Society Chairman: Dr. PO Yin Chung Speaker: Dr. TSANG Chun Pong # Seminar Room, G/F., Block A, Queen Elizabeth Hospital, Kowloon	Dr. Y.C. PO Tel: 2990 3788 Fax: 2990 3789 2 CME Points
1:00 pm	**HKMA Shatin Doctors Network - Diagnosis and Management of Overactive Bladder** Organised by: HKMA Shatin Doctors Network Speaker: Dr. Manuel B.W. QUE # Royal Park Hotel, Shatin	Miss Viviane LAM Tel: 2527 8452 1.5 CME Points
17 7:00 pm **SAT**	**4th HKMA Sports Night** Organised by: The Hong Kong Medical Association Chairman: Dr. Cissy YU # Wan Chai Ho Choi Banquet and Seafood Restaurant	Ms. Dora HO Tel: 2527 8285
2:00 pm	**Photo Seminar: Candid Pictures and Artistic Photography** Organised by: The Hong Kong Medical Association # HKMA Dr. LI Shu Pui Professional Education Centre, 2/F., Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	Ms. Dora HO Tel: 2527 8285
18 2:00 pm **SUN**	**HKMA Certificate Course on Family Medicine 2009** Organised by: The Hong Kong Medical Association Speaker: Dr. TSE Hung Hing, Prof. Albert LEE, Dr. CHOI Kin # Lecture Theatre, G/F., Block M, Queen Elizabeth Hospital, Kowloon	Miss Viviane LAM Tel: 2527 8452 2.5 CME Points
19 7:30 pm **MON**	**Introduction to the Art of Classical Chinese Poetry Writing** Organised by: The Hong Kong Medical Association # HKMA Dr. LI Shu Pui Professional Education Centre, 2/F., Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	Ms. Dora HO Tel: 2527 8285
22 8:00 pm - 10:00 pm **THU**	**HKFMS Foundation Meeting** Organised by: The Federation of Medical Societies of Hong Kong # Council Chambers, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Paulina TANG Tel: 2527 8898 Fax: 2865 0345

Meetings

19-21/2/2009	**International Colorectal Disease Symposium 2009** Organised by: Hong Kong Society for Coloproctology & Minimal Access Surgery Training Centre, PYNEH Chairman: Mr. Michael K.W. LI & Dr. Cliff C.C. CHUNG Speaker: Local and Overseas # Hong Kong East Cluster Training Centre, PYNEH, 3 Lok Man Road, Chai Wan, Hong Kong Enquiry: Ms. Christina LO Tel: 2595 6416 Fax: 2515 3195
20-22/2/2009	**CardioRhythm 2009** Organised by: Hong Kong College of Cardiology & Chinese Society of Pacing and Electrophysiology Co-Chairman: Prof. LAU Chu Pak Enquiry: Secretariat Tel: 2899 2035 Fax: 2899 2045 Email: info@cardiorhythm.com Website: http://www.cardiorhythm.com

Courses

13-15/2/2009, 27/2/2009 - 1/3/2009, 14-16/8/2009, 11-13/9/2009, 20-22/11/2009	**Advanced Trauma Life Support (ATLS) Student Course** Organised by: Department of Surgery, Queen Mary Hospital & Hong Kong Chapter of the American College of Surgeons # The Jockey Club Skills Development Centre, C3, Main Block, Queen Mary Hospital, Pokfulam, Hong Kong Enquiry: Course Administrator Tel: 2855 4885 / 2855 4886 Fax: 2819 3416 Email: hnsrg@hkucc.hku.hk Web site: http://www.hku.hk/surgery
16/3/2009-7/5/2009	**離遠病人家居護理員證書課程** Organised by: College of Nursing, Hong Kong Enquiry: Secretariat Tel: 2572 9255 Fax: 2838 6280
8&14/2/2009 22&29/3/2009, 23&31/5/2009, 18&26/7/2009, 19&27/9/2009, 21&29/11/2009	**Pre-Hospital Trauma Life Support (PHTLS) Provider Course** Organised by: Department of Surgery, Queen Mary Hospital; Hong Kong Chapter of the American College of Surgeons & Hong Kong St. John Ambulance Association # St. John Ambulance Association, 2 Macdonnell Road, Mid-Levels, Hong Kong Enquiry: Hong Kong St. John Ambulance Association Tel: 2530 8020 Email: assn@stjohn.org.hk Web site: http://www.hku.hk/surgery
30/3/2009 - 3/4/2009, 21/9/2009 - 29/9/2009, 1/3/2010 - 9/3/2010, 28/2/2011 - 2/3/2011	**ICN Leadership for Change Program** Organised by: College of Nursing, Hong Kong Enquiry: Secretariat Tel: 2572 9255 Fax: 2838 6280
25-26/4/2009, 12-13/12/2009	**Advanced Medical Life Support (AMLS) Provider Course** Organised by: Department of Surgery, Queen Mary Hospital & Hong Kong Chapter of the American College of Surgeons # The Jockey Club Skills Development Centre, C3, Main Block, Queen Mary Hospital, Pokfulam, Hong Kong Enquiry: Course Administrator Tel: 2855 4885 / 2855 4886 Fax: 2819 3416 Email: hnsrg@hkucc.hku.hk Web site: http://www.hku.hk/surgery
11-12/9/2009, 20-21/11/2009	**Advanced Trauma Care for Nurses (ATCN) Provider Course** Organised by: Department of Surgery, Queen Mary Hospital & Hong Kong Chapter of the American College of Surgeons # The Jockey Club Skills Development Centre, C3, Main Block, Queen Mary Hospital, Pokfulam, Hong Kong Enquiry: Course Administrator Tel: 2855 4885 / 2855 4886 Fax: 2819 3416 Email: hnsrg@hkucc.hku.hk Web site: http://www.hku.hk/surgery

Answer to Dermatological Quiz

1. The preliminary diagnosis is erythema annulare centrifugum. The four classic figurate erythemas are erythema annulare centrifugum (EAC), erythema marginatum rheumaticum, erythema chronicum migrans, and erythema gyratum repens.
   In analysing these figurate erythemas (presenting as annular, arciform or polycyclic lesions), two important elements have to be looked for: namely presence or absence of scaling and rate of evolution of individual lesion. Lesions in EAC spread centrifugally to a large size within days. Lesions in erythema marginatum rheumaticum spread very rapidly within hours. Lesions in erythema chronicum migrans spread slowly within weeks, while lesions in erythema gyratum repens spread within days with bizarre configuration.

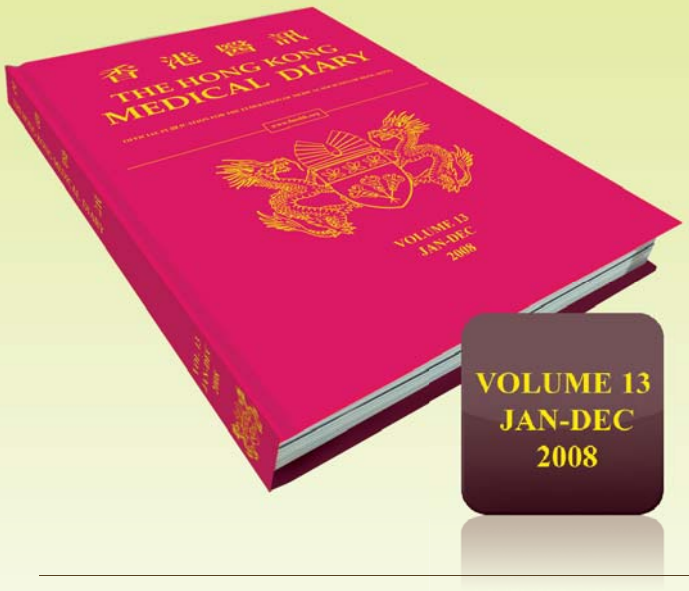
2. EAC is diagnosed by excluding other differential diagnoses, such as those above-mentioned, plus tinea corporis, annular psoriasis, lupus tumidus, subacute cutaneous lupus erythematosus, drug reaction, urticarial vasculitis, necrolytic migratory erythema, etc. There are two types of EAC. The superficial type is a distinct entity. It usually has scaling and is often associated with fungal infection elsewhere. It is believed that the lesion may be the result of allergic reaction to certain antigens. The deep type (as in this patient) is less distinctive. It usually has no scaling. In this type, lupus erythematosus and drug reaction must be excluded. Most cases of EAC however are idiopathic, and the diagnosis is usually made by exclusion.

3. Serological tests for lupus erythematosus (antinuclear factor, anti-double strain DNA, anti-Ro and anti-La), skin scraping for fungal element and culture, skin biopsy and direct immunofluorescent test should be performed.

4. Treatments are mainly symptomatic based on unproven or anecdotal reports. Topical steroid and oral antihistamine are commonly used though with limited effect in the natural course. Oral antifungals have been used empirically by some workers, especially in the superficial type. Individual lesions may persist for weeks to months.

Dr. Lai-yin Chong

MBBS(HK), FRCP(Lond, Edin, Glasg), FHKCP, FHKAM(Med)
Yaumatei Dermatology Clinic, Social Hygiene Service



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