it will not be smooth sailing. China places great emphasis on education, science and technology and maintaining high standards in the professions. At the inauguration of the Academy, representatives from China's leading medical institutions and organizations honoured us with their presence. So with the support of our colleagues and friends, especially from the well-established sister Colleges, Academies and medical centres, I am confident the Academy's objectives will be achieved.

Medical education in Hong Kong began over a hundred years ago and three medical graduates of Aberdeen University played a vital pioneering role. The Scottish tradition has persisted through outstanding medical men and women from your country teaching here, further nutured by our very close links with your College. My lecture is in honour and memory of Sir Stanley Davidson. I hope you will agree that the subject was appropriate, for Sir Stanley was a great Scotsman, physician and educationist. I am honoured to have been invited to deliver the lecture and thank you for your attention.

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THE MANAGEMENT OF CORONARY ARTERY DISEASE: A TIME FOR REAPPRAISAL

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Simple linear mathematical relationships govern most of our thinking in medicine. Even in the present day when the genes responsible for both atherosclerosis and myocardial infarction have been identified, we are lost in our age old belief that coronary artery disease is due to atherosclerosis narrowing the epicardial vessels and that the treatment is revascularisation on an acute or long term basis.

The naive thinking that the evolution in time of body organ functions depends solely on the initial conditions and that changing the initial state will have a salutary effect on the final outcome has repeatedly been proved wrong. The dynamic human body does not follow these linear relationships and doctors have been predicting the unpredictable!

With this background let us look at myocardial ischaemia. It is believed that subclinical ischaemia (so called silent ischaemia) damages the myocardium and subsequent periods of ischaemia may eventually cause an infarct. An editorial in the BMJ clearly states that this is not the case.[1] Marber and colleagues have shown by elegant studies in dogs that brief periods of ischaemia trigger adaptive changes in the myocardium protecting it from subsequent prolonged ischaemic insult.[2] This is called ischaemic preconditioning. Clinical studies have shown similar preconditioning in humans.[3] With further work I think the mist around the pathophysiology of myocardial damage will be lifted and we may be able to induce preconditioning pharmacologically.

Let us look critically at the logic of doing either angioplasty or coronary bypass grafting in patients who have an anatomic stenosis of one or more of the epicardial coronary arteries. The whole reasoning is based on two fundamental postulates: that a tight coronary block is always potentially dangerous and that attempts at revascularisation are always effective and safe.

Whereas tight stenoses of these vessels gradually progress to a complete block as time evolves,[4] the occluded vessel does not pose the risk of an infarct and its complications or even of a long term detrimental effect on ventricular function. Complete occlusion resulting in infarction is almost always the result of thrombotic obstruction of a near normal vessel.[5] In the absence of an infarct, the stenoses do not alter the long term changes in total left ventricular function despite evidence of exercise induced signs and symptoms of myocardial ischaemia.[6]

It is, therefore, likely that silent ischaemia or even the reduced blood supply due to fixed coronary lesions may be beneficial to the system by facilitating myocardial toleration of a future major failure of blood supply. The danger to those with coronary syndromes, therefore, lies in the sudden occlusion of a near normal artery producing an infarct or unstable angina, brought on by plaque disruption with consequent platelet adhesion and thrombosis.[7] If only we could unravel the mystery of this sudden clotting, we would be able to manage these

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patients better. Recently inflammation has been implicated in this process,[8] an idea which goes back to the time of Virchow. The inflammatory features were seen consistently in all plaques despite varied plaque morphology. Fuster and colleagues have shown that other factors are involved in the clot,[9] but inflammation is a new element in this field. Another field of renewed interest is that of the triggering factors—acute risk factors—that in the presence of a vulnerable plaque cause disruption and thrombosis.[10] It is also interesting that most occlusive thrombi begin on plaques which are very small and never produce angiographic blocks greater than fifty percent (<50%). This challenges the angiographers hypothesis of 'critical narrowing needing revascularisation'.[11] The second postulate that revascularisation procedures are always effective and safe rests on very flimsy grounds. No study has shown that coronary angiography is required as a 'gold standard' test in the diagnosis of coronary disease before giving the patient empirical medical therapy, whereas, on the contrary, randomised trials have demonstrated that aspirin,[12] lipid lowering regimes in individuals with high cholesterol,[13] beta blockers[14] and, more recently, angiotensin converting enzyme inhibitors[15] can save many lives.

Despite thousands of angioplasties done to date, not a single properly randomised study supports the superiority of angioplasty over medical thereapy.[16] In a randomised trial angioplasty reduced angina at six months with slightly better exercise tolerance compared with medical therapy in single vessel disease, but more patients in the first had peri-procedural myocardial infarction.[17] In patients who run the risk of sudden death as a result of coronary artery disease, bypass surgery does not afford any protection.[18] Supporting the contention that tightly stenosed vessels rarely produce an infarct and kill is recent data demonstrating that such vessels do not even reduce blood flow to the distal myocardium in patients who have no angina. There may be enough collateral supply.[19]

The Coronary Artery Surgery Study, (CASS) clearly showed that angiography should be done only to plan the operation after the decision to operate is taken and not as the basis of diagnosis.[20] If angiography is done before that decision there is a risk of the patient being frightened by the doctors that he is sitting on a 'volcano' which might kill him at any time. Much of a doctor's anxiety abut withholding from angiography can be allayed by a landmark study by Lown and colleagues in Boston[21] on second opinion for angiography which produced the conclusion:

> In a large fraction of medically stable patients with coronary disease, angiography can be safely deferred ... an estimated 50% of coronary angiographies being undertaken in the USA is unnecessary, or at least could be postponed.

The authors have been generous. In their study of 186 patients whom senior cardiologists had referred for the procedure only 3% needed angiography. For a large number of patients undergoing bypass surgery there is no evidence that it improves their prognosis compared with those managed by medical means.[22]

Disturbed coronary anatomy, except for left main artery disease, does not predict prognosis when ventricular function is good.[23] Even when those with left main artery disease who refused surgery and were followed up for over a decade, the annual mortality was only 1·3% which is not significantly higher than that of the general population and it was 0% for single and double vessel disease.[24]

Long term studies have shown that bypass grafting accelerates progression of

atherosclerosis in the proximal segments of grafted vessels along with progressive blocking of the saphenous vein.[25]

For angioplasty the restenosis rate may be as high as 50% and the blockage is due to a newly recognised disease, fibrocellular intimal hyperplasia, for which there is no remedy in sight.[26] Interestingly, patients after angioplasty do not seem to resume their previous employment as well as do medically treated patients.[27] Even the usual claim of better quality of life after bypass needs appraisal, as new thoughts on quality of life demand more critical appraisal of how it is measured.[28]

As the number of revascularisation procedures increases, it is important for doctors to appreciate that there is no direct correlation between stenoses demonstrated by angiography and the risks of morbidity and mortality. Treasure has drawn attention to the need for rethinking on this whole question.[29] The audit of coronary angiography and bypass surgery in Nottinghamshire came to the conclusion that only 49% of angiograms and 55% of bypass procedures were appropriate.[30] When obstructed internally coronary arteries are capable of remodelling themselves and of enlarging at the site of obstruction. How pleasant to recall the body's capacity to adjust to changes.[31,32] Day in and day out we are given the impression that there is an epidemic of coronary disease in the west, but a recent study by Stehbens fails to support this.[33]

I believe that the 'magic bullet' of revascularisation in coronary stenosis has not lived up to its reputation. To be fair there are two definite indications for revascularisation, intractable chest pain and poor left ventricular function with anatomic changes, such as aneurysm, ventricular septal defects or mitral leaks, making life miserable for the patient. Coronary bypass surgery is a boon to these unfortunate victims. We should encourage revascularisation based on the patients symptoms and disability rather than on 'menacing angiograms'. There is indeed a need for rethinking in this field.

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Short Report

THE EFFECT OF TESTOSTERONE ON DELAYED PUBERTY IN CYSTIC FIBROSIS

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Cystic fibrosis (CF) is associated with delayed puberty[1] of uncertain aetiology. The onset of puberty in these circumstances can be expected to improve physical status and to boost morale. The simplest way to stimulate puberty and growth is to administer physiological amounts of testosterone for up to 6 months; this is generally sufficient to stimulate bone and physical maturation to a point where pubertal development will continue spontaneously.[2]

TABLE

Measurements before and after treatment

Patients	*1*		*2*		*3*		*4*	
	Pre	*Post*	*Pre*	*Post*	*Pre*	*Post*	*Pre*	*Post*
General								
Height Velocity	3·4	6·0	3·8	7·0	8·3	6·0	5·3	7·0
Weight Velocity	5·0	−2·0	9·0	1·0	4·0	4·0	2·5	8·0
Bone age Years	10·0	12·5	11·5	13·5	10·5	12·8	11·5	14·0
Chronological age Years	14·2	15·2	14·8	15·8	13·5	14·5	14·3	15·3
Endocrine (serum levels)								
Testosterone (nmol/l)	<0·5	<0·5	0·6	<0·5	0·9	2·5	0·3	3·8
TSH (mu/l)	1·2	0·8	1·1	1·3	1·0	1·9	2·1	1·1
LH (IU/l)	2·4	4·4	1·9	1·5	2·2	—	4·1	4·4
FSH (IU/l)	<1·0	1·8	<1·0	<1·0	1·4	7·4	1·7	1·8
Respiratory function								
FEV_1 (% mean pred)	52	46	26	18	13	18	73	62
FVC (% mean pred)	66	60	47	24	32	21	70	63

General, endocrine and respiratory status of the 4 subjects before and 6 months after completion of the testosterone therapy.

FEV_1 = forced expiratory volume in 1 second (as % of mean predicted).

FVC = forced vital capacity (as % of mean predicted).

Height (cm/yr) and weight (kg/yr) velocities compare the velocities over the year immediately prior to start of therapy with the year which includes the 6 months of therapy and the six months immediately after.