Vascular Endothelium Dysfunction – Seeing an Elephant

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In the last few years, we have witnessed significant advances in the area of understanding the function of the endothelium and also on the causes and effects of endothelial dysfunction.[1]

In simple terms, the arterial endothelium comprises cells resting on a basement membrane that enact autocrine, paracrine and endocrine functions. The monolayer of endothelial cells play a crucial role in the regulation of vascular tone by the release of vasoactive substances notably NO, endothelin, prostacycline and angiotensinogen.

Endothelial dysfunction occurs very early in the process of atherogenesis, which impairs normal vasodilator response.

Endothelial dysfunction is therefore an important factor not only in atherosclerosis but also in restenosis and hypertensive heart disease. Dysfunction allows platelets to adhere to the vessel wall and in turn causes contraction by thromboxane A2 and serotonin. Platelet-derived growth factor induces migration of smooth muscle cells. Endothelial cells produce growth promoters and inhibitors. The balance between them is maintained in normal endothelial function. Under conditions of dysfunction the smooth muscle cells proliferate and migrate.[2]

Some vascular trees are more prone to the development of endothelial dysfunction like coronary arteries and aorta branches while some are relatively protected like the internal mammary artery and the brachial artery. The recognized known cardiac risk factors including age, gender, hypertension, hyperlipidaemia, diabetes mellitus, smoking, mental stress, and hyperhomocysteinaemia have been associated with endothelial dysfunction.

It is well known endothelial dysfunction can be detected well before the development of angiographically significant atherosclerotic plaque.[3]

The altered endothelial function is studied by noticing the response to ischaemia or vasoactive materials injection.

The abnormal endothelial function can be assessed in either the coronary or the peripheral arteries.

Coronary artery endothelial function is most commonly assessed by intra-coronary infusion of acetylcholine. This is based on the action via muscarinic receptors on endothelial cells and subsequent release of NO and coronary vasodilatation. The coronary endothelium-dependent vasomotion can also be studied by methods like the cold pressor test or arterial injection of papavarine or adenosine.

Even though intra-coronary injection gives an ideal of vasomotion, the invasive nature of the investigation precludes as routine test of choice. This methodology is limited primarily by the risk of the invasive procedure as well as its expense. Testing peripheral endothelium function with non-invasive technique provides an opportunity to evaluate large patient population.

Brachial artery imaging with high resolution ultrasound during reactive hyperaemia is now a widely used method of determining peripheral vascular function.[4-6]

Typically this methodology involves causing fore-arm or hand ischaemia induced by interrupting arterial blood supply with a blood pressure apparatus cuff inflation to supra-systolic pressure and the subsequent release of cuff pressure. his induces reactive hyperaemia produced by the dilatation of distal microvasculature. he measurement of the vessel diameter before and after the test reveals magnitude of the change.[7]

Abnormalities in peripheral endothelial function correlate with the presence of coronary vasomotor dysfunction. The correlation in endothelial function in both the coronary and the peripheral vasculature suggests that a common pathway contributed to endothelial dysfunction in both vascular beds.[8-9]

Endothelial function has rapidly grown into a widely used research tool. However, the lack of large data demonstrating that vascular function testing contributes specific and independent prognostic value continues to limits its clinical utility.

In addition to brachial artery imaging and coronary vasomotion to acetylcholine, Chon et al have demonstrated that vascular relaxation can be assessed by the principle of Windkessel model of the circulation, from which two separate components of compliance can be defined, and it is a simple repeatable, procedure. It is done with the CVProfilor DO-2020 System. It is capable of obtaining blood pressure measurements based on an oscillometric method as well as recording 30 seconds of blood pressure waveform data by means of a custom-designed arterial pulse pressure (or waveform) sensor which is attached to a special holding and positioning apparatus.[10]

Cellular adhesion molecules which play key role in leukocyte adherence and trans-migration are expressed on the surface of dysfunctional endothelium. They are shed into the circulation. Hence elevated levels of these circulating proteins have been observed with atherosclerosis and may be a marker of increased cardiovascular risk.[11]

Elevated levels of high sensitive C-Reactive protein, a systemic maker of inflammation have also been shown to predict the presence of endothelial dysfunction.[12]

Metabolites of NO are excreted in the urine thereby suggesting that measurements of the levels of these compounds may be reflection of dysfunction.[13]

Further antioxidant enzyme systemic superoxide dismutase is substantially reduced in the atherosclerosis. Hence, measurement of this compound is being evaluated as a marker of dysfunction.[13]

The clinical utility of the endothelium function assessment as anticipated has come from recent studies demonstrating to provide prognostic value independent of that provided by assessment of the traditional cardiovascular risk factors as evinced by recent studies.

Significantly more cardiovascular events were noted in subjects with impaired coronary artery endothelium function during the follow up period. An increase in cardiovascular events occurred in patients with normal coronary angiography but with significant endothelial dysfunction. It has been shown that presence of well preserved vasoreactivity predicts the absence of coronary artery disease and good exercise tolerance.[14] Further impaired flow-mediated dilatation has also been shown to independently predict post-operative outcome in high risk patients even after correcting for cardiovascular risk factors.[15]

Interestingly forearm endothelial function has been shown to be a marker of long-term cardiovascular events in patients with hypertension.[16]

It is exciting to observe enhanced endothelial function in response to an intervention. This enables to identify a group of patients who have an improved cardiovascular prognosis.[17-20]

However still the link between improved endothelial function and clinical cardio vascular outcome remain debatable, and probably larger prospective studies with varied patient population are perhaps needed to be more emphatic of the benefits of intervention on endothelial dysfunction.

To conclude:

a. Even though the new non-invasive modalities of assessing cardiovascular risk like quantification of coronary artery calcification by electron beam CT and measurement of carotid artery intima-media thickness have been recognized to have prognostic implications, the physiological testing of endothelial function evolves into a helpful tool to assess endothelial dysfunction.
b. Assessment of flow mediated dilatation will be useful to identify patients who are at higher risk for cardiovascular events.
c. Patients with normal coronaries by angiography with abnormal stress ECG or stress echocardiography or abnormal nuclear imaging, with abnormal endothelial function form a subgroup of patients who need aggressive medical therapy.
d. One can therefore envisage that the test may be used in primary prevention setting.
e. Repeatable nature of the test makes the test valuable in monitoring the response to various form of therapy.
f. It has potential application but then, the test requires further long term, large scale study before they are routinely practiced in the patient evaluation.

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Correct Answers

1. d
2. c
3. a
4. c
5. c
6. a
7. d
8. a & c

Chapt 172 : Pregnancy and Urinary Tract Infection

Deepak S. Ray

1. Which of the following is not a reason for increased incidence of pyelonephritis in pregnancy?
   a. Ureteral dilation due to progesterone
   b. Mechanical obstruction by pregnant uterus
   c. Increased incidence of UTI in pregnancy
   d. Glycosuria

2. E. coli is responsible forUTI during pregnancy in
   a. 50 to 60% cases
   b. 60 to70% cases
   c. 70 to 80% cases
   d. 80 to 90 % cases

3. Signif cant bacteriuria suggests
   a. More than 100 organisms per ml of cultured urine
   b. More than 1000 organisms per ml of cultured urine
   c. More than 10,000 organisms per ml of cultured urine
   d. More than 1,00,000 organisms per ml of cultured urine

4. Asymptomatic bacteriuria if untreated leads to acute pyelonephritis in
   a. 10 to20% cases
   b. 20 to 40% cases
   c. 40 to 60% cases
   d. 60 to 80% cases

5. T e following is the gold standard for diagnosis of asymptomatic bacteriuria
   a. Urine culture
   b. Leucocytes esterase agent strip
   c. Presence of pus cells
   d. Presence of nitrate

6. T e following antibiotic can be safely used for UTI in pregnancy
   a. Nitrofurantoin
   b. Ciprof oxacilin
   c. Tetracycline
   d. Sulphonamide

7. Pyelonephritis is most common in
   a. First trimester
   b. Second trimester
   c. T ird trimester
   d. Immediate post delivery

8. T e following organism causes neonatal sepsis in immediate post delivery period
   a. E. coli
   b. Proteus mirabilis
   c. Group B Sreptococcus
   d. Klepsiella pneumonae

Correct Answers

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

Section: GERIATRICS

Chapt 173 : Retarding Aging - Healthy Aging

G S Sainani, Rajesh Sainani

1. In elderly persons endocrine glands reveal
   a. Same function as in youth
   b. Hyperfunction
   c. Hypo-function

2. In andropause, testosterone levels are
   a. High
   b. Low
   c. Same as in youth

3. In somatopause, growth hormone secretion is
   a. Low
   b. More
   c. Same as in youth

4. In Alzheimer's disease, memory loss is due to
   a. Loss of cholinergic cells
   b. Loss of adrenergic cells
   c. Loss of both cells

5. Sarcopenia in elderly is related to
   a. Increased secretion of GH and IGF-1
   b. Decreased secretion of GH and IGF-1
   c. None of the above

6. Prolongation of life span can be achieved by
   a. High calorie diet
   b. Normal calorie diet
   c. Low calorie diet

7. Life span can be prolonged
   a. Single gene alterations
   b. Double gene alterations
   c. None of the above

8. Mortality in the elderly increases when there is
a. Shorter average telomere length
b. Longer average telomere length
c. Normal average telomere length

9. For healthy aging, what is important?
a. Genes
b. Healthy diet including anti-oxidants
c. Physical exercise
d. Family and social support
e. All above

10. What are the most consistent predictors of healthy aging
a. Low BP
b. Low glucose levels
c. Abstinence of smoking
d. Normal weight
e. All of the above

Correct Answers

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

Chapt 174 : Diabetes in Elderly

TK Biswas, Sobhan Biswas, Arindam Biswas

1. Age of onset of elderly diabetes is:
a. 55 years and above
b. 60 years and above
c. 65 years and above
d. 70 years and above.

2. Incidence of IDDM in elderly
a. 2.4% b. 4.8%
c. 5.4% d. 6.8%

3. Most common mode of clinical presentation of elderly diabetes.
a. Vague symptoms
b. Neurological complication
c. Polyuria, polydipsia and polyphagia
d. Coma

4. Most important diagnostic criteria for elderly diabetic is
a. Glycosuria
b. Fasting plasma glucose of 140 mg/dl
c. Random plasma glucose of 180/dl
d. 2 hours post-prandial glucose of 200 mg/dl.

5. Which is the most common complication of elderly diabetic?
a. HONK coma b. Renal
c. Cardiovascular d. Neurological

6. Mortality in elderly diabetic is most commonly related to
a. Age
b. Associated co-morbid disease
c. Hypertension
d. Diabetic foot.

7. Which type of exercise is best for elderly diabetic?
a. Running b. Tennis playing
c. Yoga Exercise d. Swimming

8. Which of the following OHA is best for diabetic control in the elderly?
a. Glimepiride b. Glyclazide
c. Metformin d. Pioglitazone

9. Which type of insulin is most preferred in elderly diabetic?
a. Human soluble insulin
b. PZI
c. Long acting porcine insulin
d. Long acting insulin analogue – Glargine

10. Which type of hypertension is most common in long standing elderly diabetic?
a. Renal hypertension
b. Essential hypertension
c. Endocrinal hypertension
d. Obstructive uropathy

Correct Answers:

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

Section: MISCELLANEOUS

Chapt 183 : Current Concepts in Conscious Sedation

S Galwankar, Kelly P O'Keefe, James R Meredith

1. The safest route for conscious sedation (CS) is
a. Oral
b. Rectal
c. Intravenous
d. Intramuscular
e. Intranasal

2. Fentanyl is
   a. 10 times as potent as morphine.
   b. Associated with histamine release.
   c. Reversible by flumazenil.
   d. Associated with rigid chest wall.
   e. Associated with resistance

3. True or False: The American Society of Anesthesiologists recommends that patients must be less than Class V to undergo CS.

4. Which is not associated with midazolam?
   a. Anterograde amnesia
   b. Analgesia
   c. Sedation
   d. Muscle relaxation
   e. Anxiolysis

5. Propofol is different from other sedatives because it
   a. Has an antiemetic property.
   b. Is not associated with respiratory depression.
   c. Rapidly induces sedation.
   d. Has pain upon injection.
   e. Requires concomitant use of atropine

6. Nitrous oxide is contraindicated in all except
   a. Pneumothorax
   b. Eye injuries
   c. Child
   d. Altered level of consciousness
   e. Obstructed viscous

7. The emergence phenomenon is associated with
   a. Midazolam
   b. Propofol
   c. Etomidate
   d. Pentobarbital
   e. Ketamine

8. The treatment of rigid chest wall includes
   a. Naloxone
   b. Flumazenil
   c. Paralytics and Ventilation
   d. Diazepam
   e. Morphine

9. Meperidine is a poor choice for CS for the following reasons except
   a. It induces seizures
   b. It causes hypertension
   c. It has unpredictable sedation
   d. There are better alternatives
   e. Fatal reactions occurred with MAOIs

10. What drug has analgesic, amnesic, and sedative properties?
   a. Ketamine
   b. Midazolam
   c. Fentanyl
   d. Pentobarbital
   e. Etomidate

Correct Answers:

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