The Microcirculation –
A New Frontier in Good Circulatory Health

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Topics for This Evening

- The importance of a healthy microcirculation
- Herbs for a healthy microcirculation
What is the Microcirculation?

- Small arteries
- Arterioles
- Capillaries
- Venules
- Small veins

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The Vascular Endothelium

- Delicate monolayer of cells lining all blood vessels
- Regulates the contractile and proliferative state of the underlying smooth muscle cells
- Regulates the interaction of the blood vessel wall with the circulating blood
Microvascular Physiology

- Small arteries and arterioles dilate or contract to maintain a constant flow of blood.
- Capillaries are able to regulate their flow by transmitting signals to upstream controlling arterioles.
- A multitude of factors influence the contraction or relaxation of arterioles (such as innervation, insulin, melatonin, blood viscosity, metabolites), but a key factor is nitric oxide (NO).

Nitric Oxide

Capillary Blood Flow

- In addition to the arteriolar control of capillary blood flow, other key factors are at play:
  - Hematocrit
  - Blood viscosity
  - Red blood cell deformability/aggregation

“The fundamental role of microvessels is to supply target tissues with oxygen and nutrients; therefore it appears logical that microvascular disorders will impact on tissue function, given the close coupling between flow and metabolism.”

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<tr>
<th>Overweight/obesity</th>
<th>Cardiometabolic syndrome</th>
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<td>Diabetes</td>
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<td>Alzheimer’s disease</td>
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<td>Venous insufficiency</td>
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<td>Myocardial infarction, stroke</td>
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<td>Hemochromatosis</td>
<td>β-thalassaemia</td>
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<td>High ferritin</td>
<td>HIV</td>
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Liver disease in general
Kidney disease
Neuropathies/neuralgias
Restless leg syndrome
Osteoarthritis (OA)
Retinal diseases
Poor healing of any tissue
Soft tissue injury
Intervertebral disc damage
Recovery from ischemic damage
Anti-aging
Heart Disease and Microcirculation

- Coronary microvascular dysfunction is under intense investigation because of the growing awareness of its importance.

- In patients with chest pain and a normal angiogram, coronary flow reserve (a measure of microvascular health) is a comprehensive indicator of cardiovascular risk.

Lee DH, Youn HJ, Choi YS et al. Coronary flow reserve is a comprehensive indicator of cardiovascular risk factors in subjects with chest pain and normal coronary angiogram. Circ J 2010; 74(7): 1405-1414
The Liver and Microcirculation

Major changes in liver microcirculation with age:
- increased endothelial cell thickness
- reduced numbers of pores (fenestrations)

Thought to contribute to dyslipidemia, vascular disease, liver degeneration and poor drug metabolism

Diabetic microangiopathy is probably the best known clinical expression of microvascular disease

- Retinopathy, nephropathy, neuropathy
Chicken or Egg?

- Type 2 diabetes (T2D) ⇒ microvascular disease
- Growing school of thought that microvascular dysfunction is the fundamental CAUSE of insulin resistance

Retinal vascular calibre is one of several surrogate measures of microvascular dysfunction.

Obesity significantly linked to narrower arteriolar and wider venular calibers.

A meta-analysis, 44,000+ individuals.

“These data indicate that various estimates of microvascular dysfunction were associated with incident T2DM and, possibly, impaired fasting glucose, suggesting a role for the microcirculation in the pathogenesis of T2DM.”

The prevalence of T2D in India is relatively high and with poor glycemic control (average HbA$_{1C}$ 9.2%). Yet eye complications (such as retinopathy) are only 16.6%\(^1\). Compared to Europe, Japan, the US and Australia at around 30%\(^2\)

Mohan V, Shah S, Saboo B. J Assoc Physicians India 2013; 61(1 Suppl): 12-15
Definition of Incretins

“Gut derived factors that increase glucose-stimulated insulin secretion”

In • cre • tin

Intestine  Secretion  Insulin

Contribution of Fasting & Post Prandial Glycemia to A1C

Monnier L et al. *Diabetes Care* 2003;26:881
Incretin Hormones

- Produced by GI tract in response to incoming nutrients
- Stimulate insulin secretion
- Discovered when insulin response to oral glucose was noted to exceed response to IV glucose
- Incretin hormones:
  - Glucagon-like peptide 1 (GLP-1)
  - Gastric inhibitory polypeptide (GIP)

The Upper GIT is a Tasting Organ

Modified from:
Upper Gastrointestinal Effects of Bitters

Bitter Taste and Metabolic Function

- In epidemiological studies, functional variants in bitter taste receptors have been linked to alcohol dependency, adiposity, eating behavior disinhibition and body-mass index.

- Generally, people with lower bitter tasting sensitivity exhibited the poorer health measure.

- The presence of bitter receptors on enteroendocrine cells suggests the mechanism behind these effects.

2 Tepper, B.J. et al. 2008, Obesity (Silver Spring) vol. 16, no. 10, pp. 2289-2295.