

# CURRENT ISSUES IN GERIATRICS-4

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**PREFACE**

The number of elderly is rising all over the world including India. The population of elderly persons in our country is around 90 million. It comprises people who have given their best during their productive years to the Society and to the Nation. These people are still a part of our main stream which is being benefited by their experience. However it is pathetic to see many of them are not cared. In the words of Victor Hugo, 'the misery of a child is interesting to a mother, the misery of a young man is interesting to a young woman, the misery of an old man is interesting to no body'. The elderly is living in a private Universe of physical weakness and mental decay. The words of Jonathan Swift remind us that 'everyone desires to live long, but no one would be old'.

There is a great need to focus our attention towards their medical and health needs. The big number of geriatric population is increasing day by day; year after year. Goethe has said, 'No skill or art is needed to grow old' the trick is to endure it'. The physician has to strive not to put more wrinkles in their minds than their faces.

Since ageing appears to be the only available way to live a long time, and the number of geriatric population is on increase in the country, there is an urgency to address the health issues of this growing mass of population as a separate segment. In advancing years many age-related disabilities begin to appear. Mobility suffers, hearing gets impaired; there is gradual loss of eye sight and loss of memory. The immunity declines making elderly persons more vulnerable to infections. Diabetes, heart diseases, cancer, enlarged prostate, Parkinson's disease, and Alzheimer's disease make their appearance. Often there is fall making them bed-ridden. Hence the aged require special medical attention. At the same time we must remember that 'there are no diseases of the aged, but simply disease among the

The rapid strides in the medical science, has enabled a steady increase in human life expectancy. The implications are that ageing is becoming a matter of concern because of the rapidly growing number older persons putting enormous pressure on health care service. Benjamin Disraeli jokingly has said, 'youth is a blunder, manhood a struggle, old age a regret'. Our aim is to take care of them through separate clinics and hospitals catering to the needs. If it is done with all seriousness the old age becomes a happy state in the life of every individual.

It is worth remembering the words of Tryon Edwards that 'some men are born old, and some never seem so. If we keep well and cheerful we are always young, and at last die in youth, even when years would count us old'

The words of James Cricton-Browne remind us that 'there is no short-cut to longevity. To win it is the work of a life time, and the promotion of it is a branch of preventive medicine'.

The annual conferences of Geriatric Society of India (GSI) were held at Gulbarga (now Kalaburagi) in 2007, Secunderabad in 2008 and Belgaum (now Belagavi) in 2010. I was associated in bringing out the presentations made during the conference in the form of book. Now the mid-term conference of GSI is being held at Vijayapura and leading academicians and geriatricians have contributed to produce this book. I express my gratitude to all contributors who have made this project a success. My thanks are to my editorial team who helped me at every stage in the production of this book.

Kalaburagi  
Feb 29, 2016

**P S Shankar**

## CONTENTS

<b>Preface</b>		
1.	Geriatrics in Indian Scenario	<i>Dr. OP Sharma</i> 1
2.	Wellness in the evening of life	<i>MS Sridhar</i> 10
3.	Hopes for Alzheimers	<i>Arvind Ghongane</i> 15
4.	Hypoglycaemia & Hyperglycaemia in the long term care of elderly diabetics	<i>MV Jali</i> 22
5.	Sarcopaenia as a geriatric syndrome	<i>PS Shankar</i> 29
6.	Delirium in the Elderly	<i>Prabha Adhikari</i> 39
7.	Morphology of Hematologic disorders in elderly	<i>Karuna Rameshkumar</i> 46
8.	Falls	<i>Sanjay Bajaj</i> 55
9.	Importance of influenza in old age	<i>AK Prasad</i> 64
10.	Can Yoga Protect Vascular Integrity in Aging?	<i>Satish G. Patil, Kusal K. Das</i> 69
11.	Addressing polypharmacy in elderly !!	<i>Sandeep P Tamane</i> 79
11.	Gero Pharmacology	<i>CG Keshava Murthy</i> 89
12.	Comprehensive Geriatric assessment : Revisited	<i>Pratibha Pereira, Basavanna Gowdappa, Suresh Rao</i> 96
13.	Preoperative evaluation and management in geriatric patients	<i>SK Gulati, Dishant Gulati</i> 107
14.	Nursing issues related to elderly	<i>Asha Shetty</i> 118
15.	Home care model for person living with dementia	<i>Ambali AP</i> 123



decline in vascular function and its integrity is the major event that most often impacts on the health of elderly people and longevity. This change in vasculature substantiates the increase in prevalence of clinical & subclinical CV diseases with age, making CV disease as the most common cause of death among the elderly [2]. Sir William Osler stated long ago that "Longevity is a vascular question, which has been well expressed in the axiom, that man is only as old as his arteries; to a majority of men death comes primarily or secondarily through this portal" [3].

Patients with hypertension and CV disease are often associated with multiple co-morbidities. They require multiple drug therapy leading to increase adverse effects and the cost of treatment. Therefore, an alternative holistic approach that controls/reduces the aging effect on vasculature with least adverse effects and cost of therapy is the need of the hour. Aging is inevitable. However, preventing vascular damage with advancing age and maintaining vascular integrity within physiological limits may promote 'healthy aging' and 'quality of life'. Vascular aging is a natural process that can be modified by physiological approaches. Several studies have shown beneficial effects of yoga based approach on CV health [4-6]. Yoga is emerging as an important lifestyle modality for prevention and management of CV risk. In this review, first, a short overview on pathophysiology of vascular senescence will be given and then the possible control of vascular dysfunction and protection of vascular integrity with yoga based approach in elderly is discussed.

### 1. Vascular function and integrity in aging

The arterial wall is comprised of three layers: *tunica intima* (inner layer), *tunica media* (middle layer) and *tunica adventitia* (outer layer). Tunica intima constitutes a single layer of endothelial cells lining the interior surface of the blood vessels. It is a key determinant of vascular homeostasis and its integrity. Tunica media constitutes circularly arranged vascular smooth muscle cells (VSMCs) embedded in their own product: extracellular matrix (ECM). It maintains vascular tone which is regulated by *tunica intima*. *Tunica adventitia* is the outermost layer made up of connective tissue predominantly with fibroblasts. Co-ordination of several complex interacting molecular mechanisms and physiological systems are essential to maintain vascular homeostasis, integrity and health.

Perturbations in these complex regulatory mechanisms results in vascular disease. The cells of the arterial wall secrete several products such as vasoconstrictors, vasodilators, growth factors, cytokines and extracellular matrix, all of which contribute to vascular homeostasis. These components and autonomic nervous system mainly regulate the vascular function. The interactions among vascular cells are substantially involved in the vascular health and disease [7].

Aging has been defined as a decreased ability to resist cellular stresses and insults. Vascular aging is characterized by gradual decline in function and morphological changes in its wall resulting in decrease in vascular compliance and elevation of vascular resistance. The sequence of changes in the vasculature with advancing age is depicted in Fig 1. Increased vascular resistance is the hallmark in the development of hypertension in elderly. The normal vascular aging process is superimposed by pathological aging changes contributing to increased prevalence of atherosclerosis. The major functional and structural changes associated with vascular aging are endothelial dysfunction and increased arterial stiffness, which are mainly implicated in the development of CV diseases in elderly individuals [8].

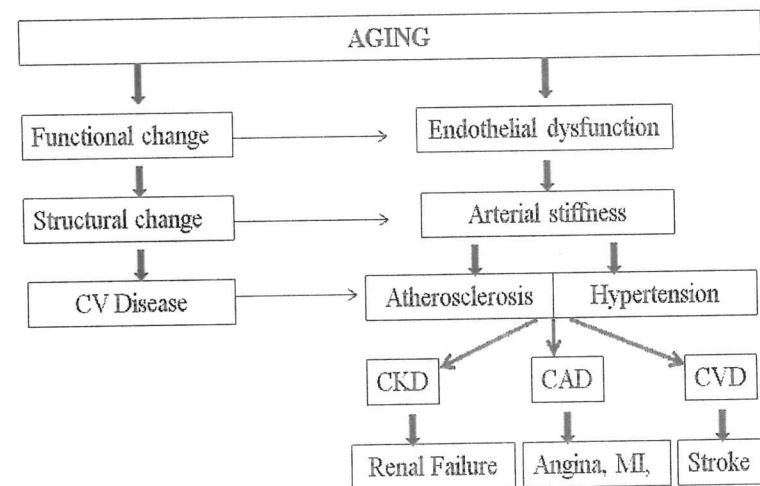


Fig 1: Vascular aging: Sequence of changes in vasculature and its consequences. CV: Cardiovascular, CKD: chronic kidney disease, CAD: coronary artery disease, CVD: cerebrovascular disease, MI: myocardial infarction.

### 1.1. Endothelial dysfunction in aging

Endothelial cell structure and functional integrity are important for various vital cardiovascular functions and integrity [7]. The endothelium is involved in a multitude of physiological functions, including regulation of perfusion, fluid and solute exchange, haemostasis and coagulation, inflammatory responses, vasculogenesis and angiogenesis. Dysfunction of endothelium is the hallmark of vascular disease in advancing age [9].

Endothelial cells secrete several products such as vasoconstrictors, vasodilators, procoagulant factors, antithrombotic factors, growth factors, matrix products and inflammatory mediators. Among these products, a key molecule that regulates most of the vascular functions and maintains vascular homeostasis and integrity is nitric oxide (NO). NO is synthesized by nitric oxide synthase (NOS) which exist in three isoforms. The NO is produced in a range of cell types within the vasculature such as platelets, macrophages and endothelial cells and outside the vasculature in neurons and inflammatory cells. In endothelial cells, NO is synthesized by endothelial nitric oxide synthase (eNOS) from L-arginine which requires nicotinamide adenine dinucleotide phosphate (NADPH) oxidase and molecular oxygen as co-substrates and co-factors such as tetrahydrobiopterin (BH<sub>4</sub>), flavin mononucleotide (FMN), flavin adenine dinucleotide (FAD), Ca<sup>2+</sup>-calmodulin and heme [10].

Sufficient bioavailability of NO is critical to normal endothelial function. It regulates vascular tone, vascular relaxation, vascular permeability and antithrombotic properties. Insufficient NO production/bioavailability is associated with all major CV risk factors such as hypertension, diabetes, hyperlipidemia and atherosclerosis [11]. The bioavailability of nitric oxide decreases with advancing age resulting in endothelial dysfunction. Nitric oxide being strong vasodilator, its reduction in production/availability results in decreased endothelial-dependent vasodilatation, increased vascular tone and vascular resistance. These changes are attributed for the development of hypertension in elderly. Reduced endothelial-dependent vasodilation forms the earliest indicator of CV diseases including diabetes and hyperlipidemia.

### 1.2. Increased arterial stiffness in aging

The major structural changes with advancing age that take place in wall of elastic arteries are stiffness and dilatation. The principal

structural change occurs in the intima (hyperplasia) and the media (degeneration) of large elastic arteries. The structural changes in the media of elastic arteries includes an increase in collagen content and cross linking, increase in elastin fragmentation and decrease in elastin content [12]. Arterial stiffness results in decline or failure in expansion of aorta in response to ventricular systole leading to elevation in systolic blood pressure (SBP), and failure to recoil results in reduction in diastolic blood pressure (DBP), thus causing widening of PP [13]. Therefore, the pattern of blood pressure (BP) in elderly is different from that of young or middle-aged adults. In elderly, SBP increases while DBP either decreases or remains unaltered, termed as isolated systolic hypertension (ISH). Moreover, arterial stiffness is an independent and strong predictor of CV morbidity and mortality in hypertensive [14, 15] and well-functioning elderly individuals as well [16].

### 1.3. Mechanisms of vascular dysfunction in aging

Several complex mechanisms contribute to development of vascular dysfunction with reduced NO production/availability with aging. Major factors that contribute to vascular dysfunction in aging are oxidative stress, inflammation and sympathetic overactivity. Decreased expression of eNOS, deficiency of eNOS substrates and co-factors such as L-arginine and Tetrahydrobiopterin (BH<sub>4</sub>), and presence of eNOS inhibitors such as asymmetric dimethylarginine (ADMA) substantiates decreased production of NO with advancing age [17-20].

Increased accumulation of reactive oxygen species (ROS) with advancing age results in oxidative stress. Superoxide can scavenge NO to form peroxynitrite resulting in nitrosative stress and thereby reduce the effective concentration of NO in endothelial cells. Further, increased oxidative stress alters the function of eNOS, where it produces superoxide instead of NO (eNOS uncoupling), which substantially reduce the bioavailability of NO contributing to endothelial dysfunction. Increased vascular oxidative stress is also attributed to increased activity of NADPH oxidase and mitochondrial production of ROS [21]. The deleterious effect of ROS is detoxified by antioxidant defense system. Superoxide dismutase (SOD), an antioxidant enzyme that detoxifies superoxide radical by converting it into hydrogen peroxide, determines the release of biologically active NO. Reduced

activity of SOD with aging increases the superoxide level which inactivates the biologically active NO [22].

ROS influences cardiovascular structure and function by modulating cell growth and inflammatory responses via reduction-oxidation-dependent signaling pathways. Vascular oxidative stress causes thickening of the vascular media by promoting smooth muscle cell proliferation and hypertrophy with collagen deposition resulting in narrowing of vascular lumen [21].

A normal inflammatory response is needed to preserve the vascular integrity. But, with advancing age vascular inflammatory response increases leading to pro-inflammatory state which forms the basis for most age-related diseases. Excessive ROS production can also induce an inflammatory response suggesting a close association between oxidation and inflammation. Chronic low grade inflammation is associated with most age-associated CV diseases including diabetes [23].

## 2. Yoga and vasoprotection in aging

Yoga has an established CV health benefits and is emerging as an important lifestyle modality for prevention and management of CV risk. It is evident from the studies that yoga practice can reduce oxidative stress and enhance antioxidant defense in subjects with CV risk factors such as hypertension and type-II diabetes. We observed a significant reduction in serum malondialdehyde (MDA) level, a marker of oxidative stress by 20.54% in elderly hypertensives with yoga practice for three months [24]. Other studies have reported nearer to 20% reduction in oxidant level in type-II diabetic subjects following yoga practice for three months [25, 26].

Our study has revealed that yoga can increase antioxidant level which was found to decline with aging. We have reported that yoga can enhance antioxidants such as superoxide dismutase (SOD) activity by 31.35%, glutathione by 20.45% and vitamin C by 9.89% following yoga program for three months [24]. This improvement in antioxidant defense system may be due to increase in the up regulation of endogenous antioxidants and/or decreased rate of its utilization due to lowering of oxidative stress with yoga practice. Precise mechanism remains unclear, but certainly yoga induced achievement in antioxidant capacity can help to cope with deleterious effects of ROS and prevents

further damage to cardiovascular cells and protects vascular integrity. Yoga induced elevated SOD level detoxifies superoxide and prevents peroxynitrite formation and thereby reduces nitrosative stress.

Reduction in superoxide level increases the production and bioavailability of NO, a key molecule that protects vascular homeostasis and integrity. Recently, we have shown that yoga can enhance the availability of NO in elderly individuals with mild hypertension [27]. This yoga induced enhancement in NO availability may be possibly through reduction in oxidative stress and improvement in antioxidant defense system.

The L-arginine NO pathway can be enhanced through regular yoga practice/physical activity which can reduce oxidative stress. It is evident from a cohort study that yoga can enhance endothelial-dependent vasodilatation indicating an improvement in endothelial function in subjects with coronary artery disease [28]. Conversely, in another study, 12 weeks of Hatha yoga training did not elicit any beneficial changes in endothelial function in healthy subjects [29]. These findings suggest that slow and sustained exercise associated with slow and paced breathing practice is beneficial for elderly individuals. However, further studies are warranted to explore the influence of yoga on age-related endothelial dysfunction.

Our study on yoga effects on arterial stiffness in elderly with increased pulse pressure showed a small but significant reduction in arterial stiffness in a short duration of three months [27]. A randomized controlled study on patients with coronary artery disease has showed that yoga practice (for one year) increases regression and retards progression of atherosclerosis, and reduces serum cholesterol levels. In this study, yoga group subjects required revascularization procedures less frequently than control group individuals [30].

Yoga can reduce the blood pressure and controls hypertension in elderly [5, 27, 31]. It has been demonstrated in a randomized controlled study that yoga practice for one hour daily is as effective as drug therapy in controlling blood pressure [32]. However, there are no scientific studies showing the yoga effects in elderly hypertensives associated with multiple CV risk factors such as diabetes and hypercholesterolemia.

Sympathetic over activity associated with advancing age is

attributed to the development of vascular disease and hypertension. Control of sympathetic over-activity has become a cornerstone in the management of CV disease. Yoga has the ability to control the excess sympathetic activation like beta blockers. We have demonstrated that yoga can reduce sympathetic overactivity and shifts the autonomic balance towards the parasympathetic dominance in elderly individuals with mild hypertension [27]. It is evident from the studies that slow and regular breathing elicits beneficial changes in heart rate variability (HRV) through CV reflex control system [33-35]. Yoga may control blood pressure through reduction in sympathetic overdrive mimicking the beta blockers.

Although there are few data on yoga effects on vascular function in aging, available information suggests that yoga can protect vascular integrity and promotes healthy aging. The precise yoga induced mechanism of benefit on vasculature remains unclear. We presume that yoga can protect vascular integrity possibly through modulating autonomic nervous system, ROS signaling pathways and inflammatory responses in aging.

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