23rd Annual Conference of
Indian Society for Atherosclerosis Research
&
International Symposium on Atherosclerosis –
from Bench to Bedside

Organized by: Preventive cardiology group & Department of Biochemistry

Venue: University College of Medical Sciences, University of Delhi & Guru Teg Bahadur Hospital

13-14 November 2010, Delhi (India)
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Highlights of ISARCON-2010

The 23rd Annual Conference of Indian Society for Atherosclerosis and International Symposium on Atherosclerosis from Bench to Bedside was held on 13th and 14th November 2010 at University College of Medical Sciences and GTB Hospital. The conference was marked by active participation of over 300 delegates from all over India and abroad. The conference was directed at physicians, scientists and young researchers. To ensure that the goals of the conference were effectively met, the plenary sessions and symposia were organised with the premier lectures of experts according to the theme and focus areas of the conference.

Major thrust areas of the conference were:

- Molecular biology and nanotechnology giving dimension to atherosclerosis
- Newer diagnostic techniques for assessment of atherosclerosis
- Emerging therapeutic modalities
- Holistic approach of Ayurveda in atherosclerotic diseases

Following presentation of the annual report by Secretary ISAR the conference was initiated by plenary lectures by Prof. KK Talwar, Director & Head, PGIMER, Chandigarh and Prof. Dorian Haskard from National Heart and Lung Institute, London. Dr Talwar elaborated on coronary artery disease in young while Dr Dorian enriched the delegates with mechanisms regulating blood flow, inflammation and distribution of atherosclerosis that provide the basis for the design of therapeutics. The first symposium was conducted on the role of molecular biology and nanotechnology in atherosclerosis. This symposium consisted of 5 lectures by Prof Martha Cathcart, Prof M Husain, Prof G Subramanyam, Prof PR Sudhakaran and Prof AK Dinda. The speakers covered aspects ranging from role of trace elements in atherosclerosis to medical applications of nanotechnology. The session was fruitful by giving direction to new thoughts for research in molecular biology and nanotechnology. To elaborate on the impact of natural sciences on CVD a symposium on role of ayurveda in atherosclerotic
diseases was successfully held with contributions from Prof Rakesh Maurya, Prof N Nalini, Prof LN Misra and Dr KV Pugalendi. The session provided focus on natural agents isolated from the various household and indigenous plants and their wonderful results on reducing the progression and prevention of cardiovascular diseases. Day 2 of this scientific extravaganza was marked by Dr Martha Cathcart’s plenary lecture on soluble epoxide hydrolase as a novel target for intervention in MCP-1 driven inflammation. Besides prevention and treatment, early detection of the disease is always a priority for clinicians. Therefore to focus on this area, a session on newer diagnostic techniques for atherosclerosis was organized and the enlightening lectures of Prof Rajavashisth Tripathi, Prof. ME Yeolekar, Prof. A Rosalind Marita and Prof SK Verma were applauded. The final symposium of this scientific feast was on emerging therapeutic modalities in atherosclerosis and Dr OP Yadava, Dr Anupam Prakash, Dr Deepak Jain, Dr M Zahid Ashraf and Dr MMA Faridi presented their views on various interventional and non-interventional modalities of management of cardiovascular diseases.

Another achievement of the conference was the successful conduction of a workshop on “Assessment of Subclinical Atherosclerosis: Issues beyond Framingham” which included cases elaborated with the aid of pedigrees, CIMT and echocardiography. It was a parallel session attended by a selected group comprising mainly of resident doctors.

Besides the symposia and workshop, the conference was enriched by open poster and free paper sessions where young researchers got a platform to present their work. Poster session was organized on both days in which around 40 young researchers participated. At the same time, best poster award and travel grant was provided to them as a mark of encouragement. ISAR also appreciated the young researchers work through Bala Ji and Sri Venkateswara awards. Kurup oration award was also given by the society for the premier work on atherosclerosis. Our conference was graced by Honorable Guest of Honour Dr SK Sarin, Chairman, Board of Governors and Medical Council of India whose inputs boosted the morale of young scientists.
The conference was held to summarize the current problems, development of new advances, prevention and treatment of cardiovascular diseases (CVD), as well as to identify gaps in our knowledge base that need to be addressed. The conference provided a rare opportunity for extensive discussion on various aspects of atherosclerosis and was an amalgamation of opinions of biochemists, physicians, cardiologists, molecular biologists and pathologists.
Plenary Lectures
Coronary Artery Disease in Young

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Coronary artery disease in adult patients under age 40 years is a relatively unusual phenomenon. Most studies show that only 3% of all CAD cases occur in this age group. Underlying Mechanisms Of Myocardial Infarction in the young Adult may be atherosclerosis, Coronary artery embolism, hypercoagulable states (oral contraceptives, systemic lupus erythematosis, Procoagulant/anticoagulant genetic abnormalities), congenital coronary artery anomalies, Others - coronary artery dissection, coronary artery spasm (including cocaine use), blunt chest trauma and vasculitis. In order to study the clinical presentation and conventional risk factors profile in young North Indian population, a retrospective tertiary care hospital based study from January 2005 to December 2009 was carried out. Young CAD was defined as age ≤ 40 years. A total of 102 (male 100; female 2) patients were included in the present study. Smoking was the predominant risk factor in these individuals (62.7%). Other factors were diabetes (8.8%), hypertension (19.6%), family H/O CAD in 12.7% patients. The lipid profile before use of statin was available in only 30 patients. The mean LDL was 86±36.2 mg/dl, HDL was 35.3±10.5 mg/dl, and triglyceride was 147±70.2 mg/dl. Acute ST elevation myocardial Infarction (65.8%) was the common mode of presentation, of which anterior wall myocardial infarction was seen in majority of them. Stable coronary artery disease was seen in 13.9% patients. Obstructive CAD was seen in 76.5% of patients and majority having single vessel disease (most commonly LAD). Normal coronary angiogram was found in 24 patients (23.5%) suggesting possible spontaneous thrombolysis in these patients. In young patients manifestation of atherothrombosis may be different from that of elderly. In elderly patients with CAD, advanced atherosclerosis is more commonly seen, where as in younger individuals lesser atherosclerotic lesions are noted with higher chance of acute thrombotic manifestation. With the established concept of the vulnerable plaque, the concept of vulnerable blood can be considered to refer to the prothrombotic state associated in these young patients. The precise reason of thrombosis in these young individuals is not clear and need detailed evaluation of various coagulation factors. In situ formation of a coronary thrombus may cause the occlusion responsible for an AMI; the subsequent spontaneous lysis of thrombus in some cases may explain the finding of subsequent normal angiogram. The mechanism for spontaneous thrombolysis at variable duration in different patients is not clear. Even the precise approach of management in these patients is not clear. It seems that thrombolytic therapy may be the preferred mode of therapy in those who present in the early phase. Those who are taken for primary PCI glycoprotein 11b/111a inhibitors, thrombus extraction catheter and plain balloon angioplasty may be enough. Stenting may be considered only if there is significant underlying atherosclerotic narrowing in addition to thrombus.

Blood flow, inflammation and the distribution of atherosclerosis

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Atherosclerosis is now widely seen as a chronic inflammatory disease driven by the response of macrophages to low density lipoproteins (LDL) that are deposited within the arterial wall. Our studies have used endothelial cell (EC) cultures as well as LDL receptor knock-out mice to explore the homeostatic mechanisms regulating vascular health. First, innate humoral immunity (natural IgM antibodies and complement) has been found to play a crucial role in protection from atherosclerosis, probably through enabling the safe disposal of debris particles (e.g., oxidized LDL, apoptotic cells, microparticles) and thereby preventing their arterial accumulation. Secondly, we have explored the mechanisms whereby arterial walls exposed to laminar flow are protected from atherosclerosis, whereas arterial branch points and curvatures are susceptible. This is largely due to differences in flow-related biomechanical vascular signaling, with laminar shear stress suppressing inflammatory gene expression in EC, but maintaining anti-apoptotic and anti-oxidant gene expression. In contrast, EC grown under static conditions or under complex flow patterns mimicking flow at susceptible sites express proinflammatory genes (e.g., E-selectin, VCAM-1, IL-8) that contribute to the cycle of monocyte-macrophage recruitment. Sulforaphane, a natural ingredient of Brassicaceae vegetables (e.g., cauliflower, broccoli), was found to shift EC gene expression towards that seen at protected sites, acting at least in part through the stimulation of the flow-sensitive transcription factor Nrf-2. This system offers considerable potential for dissecting the mode of action of other naturally occurring compounds thought to have atheroprotective effects, and for the design of therapeutics that activate flow-regulated protective signaling pathways.


Suman Kundu, Talat Roome and Martha K. Cathcart

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Introduction

MCP-1 is a potent chemotactic factor causing blood monocyte influx into tissues. We have shown that the intracellular phospholipase A₂, cPLA₂ is required for monocyte chemotaxis to MCP-1 both in-vitro and in-vivo. Additional studies revealed that arachidonic acid was required. We therefore investigated whether arachidonic acid metabolites are responsible for regulating monocyte chemotaxis.

Methods

Chemotaxis of primary human monocytes to MCP-1 was determined with a microchamber assay. Pharmacologic inhibitors of the cyclooxygenase, lipoxygenase and cytochrome-p450-epoxygenase enzymes were examined for their effects on chemotaxis. Effective inhibitors were then assessed in-vivo using adoptive transfer of treated mouse blood monocytes into recipient mice and then inducing...
peritonitis with thioglycollate, an irritant causing monocyte/macrophage infiltration to the peritoneum in an MCP-1-dependent manner.

**Results**

Cyclooxygenase-1/2 and 5-lipoxygenase inhibitors did not affect human monocyte chemotaxis to MCP-1. In contrast, cytochrome-p450-epoxygenase inhibitors dramatically decreased monocyte chemotaxis. To further implicate this pathway, inhibitors of the downstream soluble-epoxide-hydrolase pathway (sEH) were used to elevate cytochrome-p450 products by preventing breakdown. Surprisingly these inhibitors also significantly decreased monocyte chemotaxis to MCP-1. To confirm that products of sEH are critical regulators of monocyte chemotaxis, we added back sEH products, the dihydroxy-eicosatrienoic acids (DHETs), to monocytes that had been treated with irreversible inhibitors of sEH. DHETs remarkably restored monocyte chemotaxis. To confirm the relevance of this observation *in vivo*, sEH-inhibited mouse monocytes were assessed for MCP-1-dependent peritoneal migration. Inhibition of sEH activity significantly inhibited *in vivo* migration of adoptively transferred monocytes.

**Conclusion**

Soluble epoxide hydrolase provides critical products for monocyte chemotaxis *in-vitro* and *in-vivo*. 
Heat shock proteins and atherosclerosis

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Heat Shock proteins (HSPs) are present in cells under normal conditions but are expressed at high levels when exposed to a sudden temperature jump or other stress. They stabilize proteins and are involved in the folding of denatured proteins. High temperatures, altered PH and oxygen deprivation make it more difficult for proteins to form their proper structures and cause some already structured proteins to unfold. Left uncorrected, misfolded proteins form aggregates that may eventually kill the cell. Heat shock proteins are induced rapidly at high levels to deal with this problem. Most HSPs are molecular chaperones which aid in the transport of proteins through various compartments.

TYPES OF HSPs: Humans, fruit flies and plants have HSPs similar in sequence and structure. They are divided into several families: HSP 100, HSP 90, HSP70, HSP60 (Chaperonin) and the small HSP: HSP27.

HSP27: The small heat shock proteins, HSP20, HSP22, HSP27 and αβ crystalline are widely expressed chaperone proteins. Chaperones interact with other proteins to facilitate normal functions leading to cell survival. During exposure to oxidative stress chaperones preserve protein function by preventing denaturation and promoting proper protein refolding once the stress is alleviated. Rapid adaptation to the local environment is a major physiological role of smooth muscle cells. Small HSPs are targets for signaling pathways that regulate major cellular processes that underlie the adaptive function of smooth muscle which include contraction, proliferation, cell migration and secretion of signaling proteins.

HSP 27 IN ATHEROSCLEROSIS: Soluble HSP27 is released from arterial tissue in bigger quantities from normal vessel wall than the plaque. Plasma levels of soluble HSP27 were also lower in patients with atherosclerosis compared to healthy controls. Park et al (2006) reported lower HSP27 levels in plaques, lower levels of phosphorylation of HSP27 and higher levels of secreted HSP27 in humans with acute coronary syndrome. HSP 27 has antiproliferative effects hence reduced expression in the presence of growth factors and inflammatory mediators might favour smooth muscle growth and perhaps contribute to plaque formation. To counter these effects increased or normal levels of HSPs would be helpful. Resveratrol enhances HSP 27 expression in cultured human aortic smooth muscle and reduces proliferation.

In cardiovascular diseases HSP expression is modulated both at the lesion site and in plasma. HSP 70 has been suggested to protect vascular smooth muscle cells from oxidative aggression. Further high levels of these have been correlated with decreased intima/media thickness and low risk of coronary artery
disease. HSP 27 is expressed by both the endothelial cells and VSMCs and binds and stabilizes the actin microfilaments favouring the formation of actin stress fibres. It could also interfere with the atherosclerotic inflammatory response by inhibiting nuclear factor (NF-Kb) activation. HSP 27 can downregulate the apoptotic signaling pathway thereby increasing VSMCs resistance to proteoglycanically induced apoptosis and could thus contribute to stabilize atherosclerotic lesions. Cardiovascular attention has also focused on HSP27 which is known to have chaperoning activity, to inhibit F-actin polymerization, to protect against apoptosis and to be involved in the presentation of oxidized proteins to the proteosome degradation machinery. Overexpression of HSP27 protects cardiomyocyte against ischemic injury. Decreased expression of HSP27 in atherogenesis reflects proteolysis, lead to VSMCs degradation by apoptosis and causes plaque rupture. HSP 27 specifically associates with ER β and acts as a corepressor of estrogen signaling. Unregulated estrogen mediated transcription of vascular growth factors and cytokines might occur in the absence of HSP27 and foster atherogenesis.
Invited Speakers
Detection of inflammatory sites using adoptively transferred monocyte/macrophages in vivo.

Valentin Yakubenko, Ashish Bhattacharjee, Vinod Labhasetwar and Martha K. Cathcart

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Introduction

Current methods for tracking inflammatory macrophages in vivo have technical limitations. We have developed new methods with greater sensitivity for tracking adoptively transferred monocytes to sites of inflammation including atherosclerotic lesions.

Methods

We have utilized fluorescent labeling to track adoptively transferred mouse and human monocyte/macrophages to sites of inflammation in vivo in mice during peritonitis. Recent studies employ labeling monocytes with infrared dyes in nanoparticles to achieve signals with less interference by autofluorescence and greater sensitivity of detection.

Results

 Trafficking of adoptively transferred monocytes can be efficiently monitored by using lipid fluorescent dyes such as PKH26. Efficient tracking can be achieved for both mouse and human monocytes in vivo to inflammatory sites (e.g. peritonitis). With these methods, the adoptively transferred cells must be quantified ex vivo. In contrast, attempts to track similarly labeled monocyte/macrophage entry into the vessel wall in mice prone to atherosclerosis were unsuccessful. Very few cells were detected and detection was hampered by autofluorescence and insufficient signal. To circumvent these technical obstacles, novel nanoparticles with caged infrared dyes were used to label monocytes followed by adoptive transfer to animals predisposed to atherosclerosis (apoE -/- on a high fat diet). Atherosclerosis prone areas of the vasculature were significantly labeled by these adoptively transferred cells and easily detectable in resected aortas.

Conclusion

Infrared dye-labeled nanoparticles may prove to be useful tools for assessing monocyte trafficking in vivo to sites of inflammation. Future studies can employ delivery of drugs directly to sites of inflammation by these particles or assessing inflammatory sites in a whole animal by injection of autologous labeled blood monocytes.
Nanotechnology and its Medical Applications

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Nanotechnology represents a new approach to materials science and engineering, as well as for design of new devices and processes. They involve studying and working with matter on an ultra-small scale and encompass a range of techniques rather than a single discipline and stretch across the whole spectrum of science, touching medicine, physics, engineering and chemistry. They exploit the fact that, at this scale, materials can behave very differently from what they are in larger form.

Nanoscale devices are a 100-10,000 times smaller than human cells and are similar in size to large biological molecules such as enzymes and receptors. Hence nanoscale systems possess bimolecular interaction on both the surface as well as the inside of cells allowing them the potential to detect diseases and deliver treatment to the body in an so far unknown way. It is said that because nano-components can be made to share some of the same properties as natural nanoscale structure, it is possible to develop artificial nanostructures that sense and repair damaged parts of our body, acting like naturally occurring biological nanostructures such as the white blood cells. Nano-biotechnology can offer many medical applications today ranging from cancer treatments by attacking directly the tumor, to treating diabetes by regulating and maintaining the body’s own hormonal balance, to the restoration, maintenance and improvement of human organs and biocompatible implants.

In Nanotechnology, most of the promising applications are from Carbon Nanotubes (CNTs) which is a material of 21st century. This is currently attractive material for a diverse range of applications because of their extraordinary mechanical and electrical properties. These applications range from Medical to Nanoelectronics and Hydrogen storage. Their applications have already been demonstrated in controlled drug delivery/release, artificial muscles, polymer composites and sensors. CNTs offer a new double promise for medicine, providing better contrast agents for MRI and localized heaters that can induce a target cell death. They also offer a new approach to gene therapy, broken bone treatment, killing cancer cells and preserving healthy cells.

Nanoparticles also play an important role in the treatment of Atherosclerosis. Here the Nanoparticles play act as carriers to deliver the drug (Fumagilin) directly to the base of plaques.

The present talk will cover the fundamentals of Nanotechnology and its Medical applications which will have reference to the theme of the Conference.
Role of trace elements in atherosclerosis
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Trace elements in biological term can be defined as those occurring in body fluids at concentration below 1 microgram per weight. Trace elements concentration differences have been detected between the injured heart tissue and the non injured heart tissue in myocardial infarction. Changes in mineral concentration have been detected in hypertensive; atherosclerosis and ischemic heart disease represent a cause or an effect of the disease. Those which are essential for human life such as chromium, cobalt, copper, iodine, iron, manganese, molybdenum, selenium, zinc and those potentially toxic aluminum, arsenic, cadmium, lead, mercury and nickel.

Our experimental work rabbits and cockerels has shown that zinc, chromium and selenium cause regression and cadmium causes progression of atherosclerosis.

Microenvironment-dependent Divergent Effects of AGE on endothelial cell function relevant to angiogenesis.

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Vascular complications of diabetes mellitus accelerate atherosclerosis leading to ischemic condition. Though suppression of angiogenesis under these conditions may lead to retarded wound healing and exacerbation of ischemic condition due to delayed collateral vessel formation, increased pre retinal neo vascularisation is a major complication of diabetic retinopathy. The pathophysiological mechanisms underlying these divergent angiogenic responses in different organs in diabetic state have not been clearly understood. One of the possible mechanisms is the hyperglycemia associated formation of AGE products and their effects on endothelial cells probably through specific receptor or by altering oxidant status influencing processes critical to angiogenesis. In this presentation, results of our recent investigations suggesting that the angiogenic response of the endothelial cells to AGE products and hyperglycemia depend on its microenvironment will be presented.
Recent Advances in Application of Nanotechnology in Medicine

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The advent of a new millennium has noticed emergence of a new specialty in science, “Nanotechnology in Medicine” or “Nanomedicine”. Born from the explosion of nanotechnology research in 1990s, the field of nanomedicine generated phenomenal promise to expand and evolve with tantalizing prospects for patient care in the coming decades. Proper realization of the tremendous progress and potentials of nanomedicine is a great challenge for the biomedical scientists as well as well clinicians.

The fascination for “small, tiny cute” things is a natural phenomenon for mankind from the early civilization. The progress in science has given the power of miniaturization transforming the macro to micro and finally nano. Application of this technology in material science gave birth to nanomaterial. Then the realization came that in nanoform there is change of properties of the material. These unique properties acquired by these nanoparticles transform them to nanomachines. Utilizing the unique properties of the nonmaterial innumerable potential usage was envisaged. Many experts believe that nanotechnology will change the whole face of diagnostic and therapeutic medicine. For example, nanoelectronic devices (nanosensor) based on nanowires are emerging as a powerful platform for ultra sensitive direct electrical detection of a wide range of biological and chemical species, from proteins, DNA to drug molecules and viruses down to the ultimate level of single molecule. Selective targeting of cancer cells, macrophages, infective organisms and other cell types will eventually replace the conventional therapeutic practices of attaining minimum serum or body fluid concentration of drugs for effective action. Manipulation of cellular function, cellular and tissue microenvironment, modulation of signaling system are some of the future areas of nanomedicine which may enrich the regenerative medicine including efficacy of stem cell therapy.

The role of nanotechnology in cardiovascular imaging is expanding rapidly. The new targeted nanoparticle used as contrast agents for early characterization of atherosclerosis and cardiovascular pathology at the cellular and molecular levels might represent the next frontier for combining imaging and rational drug delivery to facilitate personalized medicine.

Plant based approach for regulating blood lipid profile in dyslipidemia levels

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Dyslipidemia is characterized by elevation of plasma cholesterol, triglycerides, low density lipoprotein and lower level of high density lipoprotein that contributes to the development of atherosclerosis. Though development of modern medicine resulted in the advent of modern pharmacotherapeutics for dyslipidemia including statins, fibrates etc., there is still a need to look for new drugs with lesser side
effects. Many plants and their products have been shown to possess antihyperlipidemic/dyslipidemic activity. The well known lipid lowering drug guggulsterone has also been extracted from a plant Commiphora mukul. As part of our continuing research to find bioactive natural products, we focused on finding the active components of the Indian medicinal plants (Withania coagulans fruits, Pongamia pinnata fruits, Coccinia grandis leaves, Musa paradisiaca flowers and Zingiber officinale rhizome), which can regulate blood lipid profile in dyslipemia levels and succeeded to find antidyslipidemic principles from them. Models used for screening were high-fat diet fed hamster model and C57BL/KsJ-db/db mice and compounds showed activity comparable to fenofibrate and rosiglitazone respectively.

d- limonene attenuates cardiovascular remodeling associated with renal injury in high fat diet and L-NAME treated rats

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Introduction: Metabolic syndrome is a cluster of cardiovascular risk factors that is responsible for much of the excess cardiovascular disease morbidity among those persons with obesity, hypertension, diabetes and is a major public health challenge worldwide. High-fat diet (HFD) and Nω-nitro-L-arginine methyl ester (L-NAME) supplementation might induce changes in energy metabolism and eventually result in obesity and metabolic disorders, endothelial dysfunction, insulin resistance, dyslipidemia, and hypertension in rodents and humans. An additively increased risk for cardiovascular disease is reported for patients with both metabolic syndrome and chronic kidney disease, although each is an independent risk for cardiovascular disease. Natural products have been used for thousands of years to treat human disease, including the symptoms of the metabolic syndrome. This study has investigated whether the supplementation with a natural product d-limonene prevents cardiovascular remodelling and renal injury in a rat model of metabolic syndrome.

Methods: Young male Wistar rats were fed HFD (42.2% beef tallow) together with L-NAME (80mg/L in drinking water) for 8 weeks to induce metabolic syndrome. Rats received d-limonene (2%) as a food supplement in the diet for the last 4 weeks.

Results: HFD-fed rats treated with L-NAME showed increased body weight, abdominal circumference, visceral fat pad, systolic blood pressure, heart rate, plasma glucose, sodium, creatinine, leptin, urine potassium concentrations, cardiac hypertrophy, left ventricle collagen deposition, with decreased plasma adiponectin, nitric oxide, potassium, urinary sodium, urine volume creatinine clearance concentrations and decreased activities of peptidases. Dietary supplementation with d-limonene attenuated the HFD and L-NAME induced cardiovascular, metabolic and renal changes.
Conclusions: These results strongly suggest that dietary d-limonene may be considered as a promising complementary treatment to reverse cardiovascular and renal changes in diet induced metabolic syndrome.

Scope of natural cardio-vascular drugs as alternative medicine
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It’s easy to forget about the body organs, as they do their job automatically. But over the years, daily abuses like stress, eating junk food, living a sedentary lifestyle, smoking, etc. slowly degenerate metabolic functions and cause serious consequences. Thankfully, all is not dismal for heart related diseases. In fact, unlike accidents and terminal illness, heart disease is usually controllable.

One of the components required for a healthy heart is proper blood circulation. It keeps the heart beating, moving blood throughout veins and arteries and providing us with the nutrients which we need to live thus preventing diseases. For effective circulation, the blood’s route through the body must be open, flexible and free of any obstruction. A whole food diet of fruits and vegetables, plenty of water and regular exercise can keep your heart and vessels fit. Since prevention is the best medicine, herbs have a lot to offer in this regard. The medicinal effect of some of the herbs is empirically proven.

There are several herbs which constitute to the alternative systems of medicine and are used as prescription drugs for heart ailments. The chemicals which are responsible for cardiovascular benefits have been worked up in case of some of the herbs. For example, Garlic (Allium sativa), Hawthorn (Crataegus oxyacantha), Cayenne (Capsicum annuum), Valerian (Valeriana officinalis), Bilberry (Vaccinium myrtillus), Ashwagandha (Withania somnifera), etc. The chemo-biological evaluation of these drugs will be discussed in this lecture.

Does type of feeding in Infancy Influence Lipid Profile in later life?
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Background: Breastfed infants have significantly less risk of developing Type-2 diabetes and coronary artery disease in adult life.
Objective: To compare lipid profile of exclusively breastfed and mixed-fed term appropriate-for-gestation age infants.

Design: Prospective comparative study.

Setting: Tertiary care hospital.

Subjects and Methods: Four hundred consecutively delivered term healthy infants, 200 on exclusive breastfeeding and 200 receiving mixed feeding, were recruited at 14 (±1) weeks of age and their lipid profile was followed till 6 months of age. Another 199 consecutive term healthy infants, comprising of 105 exclusively breastfed and 94 mixed-fed infants were recruited at 6 months (±2 weeks) of age from well baby clinic and their lipid profile was followed till one year of age. Maternal lipid profile was also done.

Results: Mean total cholesterol at 6 months age was significantly higher in exclusively breastfed group (156.38±50.42 mg/dl) than mixed-fed infants (139.5±37.59 mg/dl). Changes in total cholesterol, triglycerides and HDL-C/LDL-C from 14 weeks to 12 months of age were significant (P < 0.001) in both groups. LDL-C and triglycerides were significantly higher in the breastfed group at 14 weeks, 6 months and 9 months. The HDL-C and HDL-C/LDL-C ratio showed significantly improvement at 6, 9 and 12 months in exclusively breastfed group (P =0.045) compared to mixed fed infants. The lipid profile was comparable in all babies at 1 year of age. No relationship was found in the lipid profiles of parents and infants.

Conclusion: Breastfed babies have significantly higher TG, LDL-C and TC compared to mixed-fed babies in the first 6 months of life with improving HDL-C/LDL-C ratio and decreasing TC over one year of age. This study provides support for the hypothesis that breastfeeding helps in the development of brain in infancy and does programming for effective lipid metabolism in later life.

Total word count=296

Antiatherogenic effect of 18β-glycyrrhetinic acid, an aglycone of glycyrrhizin, in diabetic animal model

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Licorice (Glycyrrhiza glabra) has a long history as a medicinal plant and is used throughout the world. Glycyrrhizin, a triterpenoid saponin, is the main constituent of licorice root, which is composed of one molecule of glycyrrhetinic acid and two molecules of glucuronic acid. Oral administration of glycyrrhizin has been shown to be hydrolyzed by the glucuronidase of intestinal bacteria to its principal aglycone, 18β-glycyrrhetinic acid, which is absorbed into the blood. In this study, we have investigated the efficacy of 18β-glycyrrhetinic acid on glycaemic control, hyperlipidaemia, mRNA level of glucose transporters,
peroxisomal proliferators-activated receptors and protein expression of glucose transporters and also histopathological alterations in streptozotocin (STZ)-diabetic rats.

Diabetes was induced in adult male albino rats of the Wistar strain, weighing 180–200 g, by administration of STZ (40 mg/kg of body weight) intraperitoneally. Plasma glucose and glycosylated haemoglobin increased whereas plasma insulin and haemoglobin (Hb) decreased in diabetic rats. Activities of gluconeogenic enzymes such as glucose 6-phosphatase, fructose 1, 6-bisphosphatase increased in liver and kidney and glucokinase, glucose 6-phosphate dehydrogenase decreased in the liver along with glycogen. The levels of total cholesterol, triglycerides, free fatty acids and phospholipids increased in the plasma and tissues and treatment with 18β-glycyrrhetinic acid improved the above parameters towards normal levels. High density lipoprotein-cholesterol (HDL-C) decreased whereas low density lipoprotein-cholesterol (LDL-C) and very low density lipoprotein-cholesterol (VLDL-C) increased in the plasma, which is reversed after treatment with 18β-glycyrrhetinic acid. Histopathological studies also supported the biochemical findings. mRNA levels of glucose transporters-2 and 4, PPAR-α (peroxisomal proliferator-activated receptor-alpha) and PPAR-γ were down regulated in diabetic rats and on treatment significantly up-regulated the mRNA levels. Protein expression of glucose transporters (GLUT-1, GLUT-2 and GLUT-4) decreased, which significantly increased after treatment with 18β-glycyrrhetinic acid. Thus our results demonstrate that 18β-glycyrrhetinic acid decreased the plasma glucose by increasing insulin secretion, enhancing glucose uptake and modulating the lipid metabolism and thus help in assuaging the hyperglycemic condition.

**Systems biology and approaches to cardiovascular and metabolic disorders**

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Complex biological processes such as metabolic and cardiovascular disorders depend on the coordinated actions and interactions of a variety of molecular and environmental factors. Systems biology approaches include identification of the components of the complex biological systems and mathematical modeling of their dynamic interactions. These approaches provide valuable understanding of how the components function together in quantitative, temporal, and spatial manner. Modern basic biological methodologies have accelerated the identification of molecular and environmental components for common diseases such as obesity, diabetes, and atherosclerosis. Discovering components for these diseases provide novel opportunities to establish broader network of molecular interactions. Results from recent investigations have made useful efforts to develop and apply systems-based approaches to reconstruct networks underlying metabolic and cardiovascular disorders integrating genomic, molecular, biochemical, physiological and clinical data. Elucidation of networks from these data make it possible to see how the components function together in complex biological systems and provide an effective way to interpret associations between molecules and disease. Thus, reconstructed biological networks can lead to a better
definition of pathways underlying metabolic and cardiovascular diseases and to identification of novel biomarkers and most suitable targets for molecular therapies.

**Bio – markers in cardiology**

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Apart from traditional approach to the disease, which includes etiology, clinical, therapeutic and preventive aspects, a new discipline “Predictive Medicine – Bio markers and predictors” is gaining more attention particularly in Cardiovascular medicine that too in coronary atherosclerotic heart disease.

In cardiovascular medicine atrial fibrillation, congestive failure, stroke and myocardial infarction are like impending disasters and recognizing them early will decrease the morbidity & mortality associated with them.

Biomarkers are enzymes, proteins, hormones that are associated with damage to the heart. Biomarkers can be grouped as mechanistic markers, clinical disease markers & therapeutic markers, which include genetic variants, clinical images, physiological tests & tissue specimen biopsies.

Some of the biomarkers which are helpful in early recognition of presence of CAD before they clinically manifest are poor oral hygiene, increased epicardial fat thickness, Carotiplaque, decreased flow mediated vasodilatation, ankle brachial index (ABI) and increased pulse wave velocity (PWV).

Elevated hs C – reactive protein, uric acid, homocystine, fibrinogen levels & micro albuminuria predict increased cardiovascular morbidity & mortality.

CPK-MB, Myoglobin, cardiac Troponinins are helpful in early recognition of myocardial infarction and BNP in of heart failure.

Many biomarkers are still in developing phase including ischemia modified albumin, sCD40 Legand, myeloperoxidase, Nitrotyrosine, choline, pregnancy associated plasma protein – A, fatty acid bindly protein and some of them in future may provide important insights into the diagnosis & management of cardiovascular diseases.

**Translational Dimensions in Clinical Atherosclerosis**

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It is sufficiently known that the phenomenon / process of atherosclerosis is multifactorial. Addressing interventions in those who are vulnerable by the reason of multiple risk factor profile of Hypertension, Diabetes Mellitus, chronic smoking, and those susceptible due to strong family history has been one of the thrust area of clinical action.

Needless to add that those who have developed ACS indeed require aggressive intervention. Few recent observations of importance require a special consideration:

- a. The importance of measuring plaque: both progression and possible regression when placed on hypolipidemic agents as concurrent monitoring on a periodic basis, with lipid profile indicators as a realistic double check.

- b. Focussing on vulnerable unstable atherosclerotic plaque and not on concentric luminal stenosis alone, with stress on factors that precipitate plaque rupture.

- c. The failure of use of statin treatment for primary prevention of cardiovascular diseases including all cause mortality in a high risk primary prevention setup.

- d. Positive effects of niacin alone or in combination on all cardiovascular events and on atherosclerosis evolution.

Translational dimension involves integrating research inputs from basic sciences to optimize both patient care at all the disease stages and also preventive measures that may not be confined to provision of health care services alone. There exists a substantial scope for sustainable solutions to the atherosclerotic vascular disease and the NCD spectrum. The implications of the above four observations in the therapeutic practice / preventive context are significant and shall be elaborated.

**Role of PTEN mutation in atherosclerosis**

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Phosphatase and Tensin Analogue (PTEN) gene located in the long arm of chromosome 10 (10q23.3) acts as a tumor suppressor gene in mutated state. This genetic mutation is associated with cancers of ovary, endometrium, colon and breast.

PTEN is recently found expressed in endothelial, subendothelial, vascular smooth muscle cells and in cardiac myocytes. PTEN is found to play a role in regulation, apoptosis, proliferation and migration of vascular smooth muscle cells. PTEN in mutated state is implicated in the pathogenesis of atherosclerosis. Over expression of PTEN inhibited insulin derived growth factor-1 (IGF-1) induced smooth muscle cell proliferation in both saphenous vein and internal mammary artery. Suppression of PTEN also leads to greater proliferative response induced by IGF-1 stimulation.
Inactivation of the tumor suppressor gene PTEN, in smooth muscle promotes a pro-inflammatory phenotype and enhances neointima formation.

PTEN mutation can be studied using molecular analysis with Polymerase chain reaction with nuclear probes. This method is highly sensitive. In the absence of molecular analysis, PTEN mutation can also be studied using Immunohistochemistry in histopathology specimens of atherosclerotic blood vessels. There is a scope for multicentre large centre studies on PTEN in atherosclerotic vessels from India.

Understanding cardiovascular risk in the light of glitazone controversy-Recent FDA Guidelines

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Type 2 Diabetes is a common metabolic disorder characterized by chronic hyperglycemia. The morbidity and mortality associated with diabetes accounts for a substantial proportion of healthcare budget besides conferring a highly compromised quality of life for the affected individuals. The treatment goals for these Type 2 diabetic patients have evolved considerably over the last 80 years. The DCCT and the UKPDS trials have demonstrated the importance of intensive glycemic control in reducing complications such as retinopathy, neuropathy and nephropathy. However, the effect on cardiovascular disease, which is the leading cause of morbidity and mortality in these patients, has not been clearly demonstrated. It is known that sulfonylureas and insulin increase cardiovascular disease, by promoting atheroma formation. The biguanide drug, metformin is considered safe by the medical community and yet there is no evidence of improvement in cardiovascular outcome. Recent reports, on the increased incidence of adverse cardiovascular events in patients treated with the most popular drug, Rosiglitazone have given rise to new concerns for the physicians and the patients. With increasing types and number of treatments available today, for these patients, treatments that impart beneficial cardiovascular effects are preferred. It is a paradox that we have too many drugs to reduce HbA1c levels in diabetic patients but none to reduce CVD burden. In 2008, the FDA committee has issued new guidelines for industry which recommend that the clinical trials involving new treatments should thoroughly address the cardiovascular risk during development and before approval is sought. These guidelines are expected to help the patients and the caregivers towards the development of novel, effective and heart-friendly antidiabetic drugs.

CABG Vs PCI in Acute ST Elevation MI

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In contemporary practice, CABG is not considered a primary revascularization option in setting of an uncomplicated acute STEMI. Though a few studies in late 1980s and 1990s did suggest a role for CABG in acute MI, if performed within the first 3-6 hours, but with the emergence of percutaneous techniques and supportive pharmacotherapy in form of Glycoprotein IIb/IIIa inhibitors and Heparin analogues, the latter have taken over in totality from CABG. Not only the logistics and the results favour PCI, but intuitively speaking also, performing a complex surgery on a blood vessel subtending a dead or dying, irritable myocardium is not only not helpful, but may even be dangerous. Even grafting a non infarct related artery has not great benefit in acute setting. Moreover the mortality of CABG in the first 48 hours of MI can be as high as up to 10-15%. To the very contrary, primary PCI opens up the infarct related artery expeditiously and possibly without the major hazards of CABG. Therefore the primary option in acute MI in contemporary practice is between primary PCI and thrombolysis with bypass surgery and cardiac surgery being reserved for certain special situations like:

1. Mechanical complications of AMI (VSD/MR/free wall rupture)
2. Cardiogenic shock, specially when associated with left main or severe triple vessel coronary artery disease
3. Recurrent ischaemia/Infarct extension, specially if the patient is either unsuitable for PCI or has failed PCI.

Statins beyond LDL reduction

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Over the past decade, statins have emerged as the most important class of lipid-modulating agents. Through inhibition of HMG-CoA Reductase, statins restrict the rate-limiting step of cholesterol synthesis, which leads to upregulation of LDL-receptors on cell membranes, and thus reduction of atherogenic LDLS. This effect translates into reduction of cardiovascular events by 25-30%, both in primary as well as secondary prevention trials.

The reduction in relative risk of cardiovascular events achieved by statin therapy appears to be similar regardless of baseline cholesterol levels. More recently, the researchers have demonstrated a number of additional cardiovascular effects of statins, unrelated to their cholesterol-lowering property. These pleiotropic effects, seen primarily with high doses of statins, included among others – anti-inflammatory, anti-proliferative, anti-thrombotic, immuno-modulatory and anti-arrhythmic effects. Clinical studies have shown that aggressive statin therapy may result in: (i) stabilization of unstable plaques in acute coronary syndrome, (ii) regression of atherosclerosis, (iii) cardioprotection during coronary interventions, and (iv) primary prevention of cardiovascular events in high risk individuals.

At least three large randomized trials - MIRACL (2001), PROVE-IT (2004) and A to Z (2004), involving over 11,700 patients, showed 11-16% reduction in composite primary endpoint of death, MI, unstable angina, revascularization, stroke and CHF with aggressive statin therapy, compared to standard therapy in the control group. Histopathological studies have shown that high dose statins reduced the number of
high grade plaques by converting grade 6 vulnerable to grade 1 stable plaques without significant reduction in total and LDL-cholesterol levels.

Data from IVUS studies such as REVERSAL with atorvastatin (80mg) and ASTEROID with rosuvastatin (40mg) has shown the efficacy of these statins in producing regression of atherosclerosis as evidenced by significant reduction in atheroma volume and diameter stenosis on follow-up.

Beneficial effects of statins in reducing peri-procedural myocardial infarction during coronary interventions has been demonstrated in ARMYDA CAPTURE trial (2009) and NAPLES II study (2009). Both the studies have shown that administration of high dose of atorvastatin (80mg) in patients with acute coronary syndrome, receiving chronic statin therapy and undergoing coronary intervention, results in improvement in biochemical markers of myocardial injury as well as clinical outcome with lower incidence of adverse cardiac events on follow-up.

High levels of hs-CRP is believed to be a strong and independent predictor of cardiovascular events. In the JUPITER trial (2008), which enrolled apparently healthy subjects with LDL<130mg/dL but high levels of hs-CRP (>2mg/dL), rosuvastatin (20mg/day) administration resulted in 44% reduction in composite primary endpoint of MI, stroke, unstable angina, revascularization and cardiac death, and 20% relative risk reduction in all-cause mortality. The study has thus demonstrated a new role of statins in primary prevention of cardiovascular events in susceptible individuals.

In conclusion, the new emerging data has provided convincing evidence on the beneficial effects of high dose of statin therapy in several clinical conditions, uninfluenced by baseline as well as post-therapy, total and LDL cholesterol levels.

**STEMI Presenting in a Non-PCI-Capable Community Hospital- to Treat or to Transfer?**

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There is general agreement that the preferred reperfusion therapy in acute ST-elevation myocardial infarction (STEMI) is primary percutaneous coronary intervention (PCI). But what if the patient presents at a non-PCI-capable community hospital? The triage of these patients has been guided by two very recent large trials, the CARESS-in-AMI trial and the TRANSFER-AMI trial, both of which tested the pharmacoinvasive approach, comprising of fibrinolytic therapy followed by transfer for primary PCI, versus the standard treatment, which comprised of transfer only in case of failed fibrinolysis. Both the trials showed similar result, in so far as the routine, early transfer of high-risk, fibrinolytic-treated patients to a PCI centre for early PCI supported by contemporary antiplatelet and antithrombotic therapy is better then the standard treatment.
Based on this a protocol is suggested for STEMI patients presenting to a non-PCI-capable facility. The patients should be initially triaged to fibrinolytic therapy or immediate transfer for PCI and this decision will depend on multiple clinical observations that allow judgment of the mortality risk of the STEMI, the risk of fibrinolytic therapy, the duration of the symptoms when first seen, and the time required for transport to a PCI-capable facility. If primary PCI is chosen, the patient should be transferred for PCI. If fibrinolytic therapy is chosen, the patient should receive the agent(s), and a judgment as to whether the patient is high risk or not should be made. If high risk, the patient should receive appropriate antithrombotic therapy and be moved immediately to a PCI-capable facility for diagnostic catheterization and consideration of PCI. If not high risk, the patient may be moved to a PCI-capable facility after receiving antithrombotic therapy or may be observed in the initial facility.

Medical management of atherosclerosis

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Atherosclerosis is a continuous progressive process. It can have varied and at times devastating manifestations and presentations. It is paramount to aim at prevention and treatment of atherosclerosis. This encompasses control of modifiable risk factors viz. hypertension, hyperlipidemia, diabetes mellitus, and cigarette smoking.

Over the years, attention has been centred on the endothelium which is now considered to be the nodal point for generation of various inflammatory mediators and also the focus of plaque generation. In fact, evidence strongly correlates endothelial dysfunction to atherosclerosis. Recent advances in the understanding of the vascular biology of atherosclerosis raise the possibility of novel therapies which may directly address different aspects of endothelial dysfunction and modify atherogenesis.

Potential cellular targets include vascular smooth cells, monocyte/macrophage cell lines, platelets and endothelial cells. There is accumulating evidence that antiplatelet agents, antioxidant therapies, amino acid supplementation, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers may prove to prevent or slow the progression of the disease. Some studies have claimed reversal of atherosclerosis with pharmacologic agents such as statins and cilostazol, but further studies are required to justify significant benefit in reducing clinical events. Newer drugs and use of combinations can very effectively bring dyslipidemia under control.

Judicious use of effective tools to control various risk factors and endothelium-targeted therapies may help control the morbidity and mortality burden of atherosclerosis.
Oxidized phospholipids as biomarkers for diagnosis and prognosis of cardiovascular diseases. M. Zahid Ashraf, Div. of Cellular Biochemistry, Defence Institute of Physiology & Allied Sciences, Delhi, zahidma@yahoo.com

Inflammation and oxidative stress are key factors in atherogenesis and are associated with lipid peroxidation and the formation of biologically active oxidized phospholipids. Produced by enzymatic or non-enzymatic processes, oxidized phospholipids molecules interact with various cells via specific receptors and in general give rise to inflammatory signals. There is considerable evidence that oxidized phospholipids accumulate in vivo and play significant roles in atherosclerosis and thrombosis, suggesting that oxidized phospholipids could be a biomarker that reflect the global extent of these diseases in vivo. A growing number of studies suggest that, apart from elevated cholesterol levels that are already recognized as risk factor, oxidized phospholipids also play an important role in atherosclerosis. Oxidized phospholipids accelerate atherosclerosis by interacting with different receptors that mediate foam cell formation, as well as through their reactive groups that can bind covalently to proteins; forming lipid-protein adducts that become dysfunctional. Pro-inflammatory oxidized phospholipids are significant predictors of the presence and extent of carotid and femoral atherosclerosis, development of new lesions and increased risk of cardiovascular events. Thus, the oxidized phospholipids could be a diagnostic marker of coronary artery disease and may represent a potential target for therapeutic interventions.
Kurup Oration Award

Phytochemicals: Gold mine in hyperglycemia-induced atherosclerosis

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The plants synthesize a variety of phytochemicals with anti-hyperglycemic and anti-atherosclerotic potential which play a major role in protection against hyperglycemia-induced atherosclerosis. In the present study, anti-diabetic and anti-atherosclerotic activity of phytochemicals isolated from aqueous extract of fruit-pulp of Eugenia jambolana (EJ) and leaves of Cassia auriculata (CA) were investigated. Detailed UV, NMR, IR spectra suggested that purified active compound (FIIc) from EJ is α-hydroxy succinamic acid (patent granted) and compound (CA100) from CA is a coumarin derivative. The effective dose of FIIc is found to be 15 mg/kg b.wt, while of CA100 is 20 mg/kg b.wt., which exhibit glycemic control and lipid-lowering activity in STZ-induced diabetic rats. Significant observation was that their single dose exhibit glycemic control up to 48 hrs, while other drugs require daily administration. FIIc imparts blood glucose-lowering effect through improved insulin levels and control over carbohydrate metabolizing enzymes. FIIc also showed protective effect on hyperglycemia-induced oxidative stress and endothelial dysfunction and hence, it may have beneficial effect in reducing the risk of development of cardiovascular diseases. CA100 exerts anti-hyperglycemic effect through insulin response along with improvement in insulin signaling by reversal of PKC activation and GLUT4 expression and translocation. Treatment with both phytochemicals causes reversal of fatty steatosis in heart myocardium. The improved insulin levels as well as signaling and decreased activity of HMG CoA reductase by CA100 might be responsible for hypolipidemic and anti-atherosclerotic effect. LD50 of FIIc and CA100 is found to be much higher than the effective dose, thus they can be considered quite safe which is also proved both biochemically and histomorphologically.
Sri Venkateswara Cardiac Research Medal – Clinical Research on Atherosclerosis and allied aspects

Haplotype Analysis of Apolipoprotein A1 Gene Polymorphism for Effect on Serum HDL and Apolipoprotein A1 Levels

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Objective: To evaluate the effect of polymorphism in Apolipoprotein A1 gene (G-75A and C+83T) on HDL and Apolipoprotein A1 levels.

Materials and Methods: Study group consisted of 100 subjects. S. Apolipoprotein A1 was estimated by turbidometric immunoassay and HDL by enzymatic direct clearance method (SYNCHRON CX9). Extracted DNA from blood sample was amplified by PCR, digested overnight with MspI restriction enzyme, run on 8% Polyacrylamide gel and Restriction fragment length polymorphism studied by gel documentation system.

Results: At -75bp, HDL and Apolipoprotein A1 levels were significantly higher in GA genotype as compared to GG (34.75± 8.74 mg/dl, 24.64 ± 4.00 md/dl ;p<0.0001 & 94.71±11.82mg/dl, 72.98 ±14.38 mg/dl ;p<0.0001). At +83bp (C+83T) ,HDL level in CT genotype (34.84±9.55mg/dl ) was significantly higher than that in CC (28.84 ±5.58 mg/dl) & TT (23.53±3.67 mg/dl) with p<0.0001. Also, apolipoprotein A1 levels in CT genotype had significantly higher levels (93.18±13.45) than CC (87.62±15.64) and TT (66.29±8.02) with p<0.0001. On analysing HDL and Apo A1 with respect to combined genotype at both sites, it was found that GA/CT showed most favourable HDL (37.03± 8.95) and Apo A1 levels (97.55± 10.25) while GG/TT showed most unfavourable profile with lowest HDL (22.72± 3.63) and apo A1 levels (62.16± 6.39).

Conclusions: Heterozygosity at -75bp and +83bp, GA/CT genotype showed highest HDL and apolipoprotein A1 concentration. G at -75bp and T at +83bp may be susceptibility alleles for Cardiovascular Diseases However, ours being a pilot study, studies with larger sample size are needed to confirm or refute the findings.
Cardioprotective activity of *Terminalia arjuna* in isoproterenol-induced cardiotoxicity in rats

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Subcutaneous injections of the synthetic beta-adrenoreceptor agonist isoproterenol (ISO) produced infarct-like lesions of the myocardium in the rat similar to that of myocardial infarction in humans. Various experimental and clinical evidence prove that either exogenous supplementation of natural antioxidants or augmentation of endogenous antioxidants attenuates myocardial ischemia produced by isoproterenol. Although the exact molecular mechanisms of cardiotoxicity are not well established, oxidative stress produced by isoproterenol is supposed to be major culprit of this overall phenomenon. In the present study we investigated whether oral administration of hydroalcoholic extract of *Terminalia arjuna* augments the antioxidant cascade of ischemic episode.

Materials &Method: *T. arjuna* was administered orally to wistar albino rats (150 g to 200 g) in three different doses (100 mg/kg, 200 mg/kg and 400 mg/kg), by gastric gavage for 28 days. At the end of this period, normal (sham), control (ischemic) groups and *T. arjuna* - treated groups were subjected to isoproterenol (85 mg/kg b.w) subcutaneously twice at an interval of 24 hr, blood samples were collected from retro orbital plexus at 0th, 21st and 30th days. Rats were anesthetized with thiopentone sodium at a dose of 30 mg/kg intraperitoneally and hearts were incised from different groups and sacrificed immediately. Result: ischemia group resulted in significant cardiac necrosis (p >0.05), which is clearly seen in histopathological study and indicated by elevated levels of lipid peroxidation as well as marker cardiac enzymes such as serum glutamateoxaloacetate transaminase, creatinekinase-MB and Troponin I and decrease in antioxidant enzymes viz reduced glutathione (GSH), superoxidedismutase (SOD). After treatment antioxidant enzymes and marker enzymes tends towards normal and the architecture of myocardium was restored. Conclusion: The present study showed that *T. arjuna* augmented the endogenous antioxidant enzymes, suppressed the neutrophil infiltration, limited the infarct size, with concomitant reduction in serum MDA and marker cardiac enzymes significantly (p>0.05) in rats subjected to isoproterenol.
Free Papers
Role of BHUx and PTY-1 in management of diabetic complications like atherosclerosis and nephropathy

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Atherosclerosis is predominant in diabetics and its other complication includes nephropathy. In India, predominance of diabetes is continuously increasing so there is need to prevent these associated complications of diabetes. One of our patented herbal products- BHUx (EU#1583499 dated-25.6.2009, US#20060147555, ZL200380109770.X dated-17.06.2009) has been found to be very effective in preventing degree of lipid deposition and abnormal lipid profile in blood. BHUx consists of specific fraction of 5 medicinal plants namely Termenalia arjuna, Strychnox nux vomica, Boswellia serrata, Commiphora mukul, and Semecarpus anacardium. Its mechanism of action has been proved to be through FR scavenging and anti-inflammatory property. It has shown inhibition against LPS induced NO production in macrophages. In vitro studies have indicated its specificity towards inhibition of lipoxygenase-15 and cyclooxygenase enzymes. It has shown promising results in histological parameters in diet induced atherosclerosis in rabbits and in ApoE knockout mice, with reference to maintain the degree of collagen cap and reduced Ca content in existing plaque, which was further substantiated with results obtained from HUVEC cell lines. BHUx was found to be safe in preclinical toxicity study in treatment span of 90 days. Another herbal preparation PTY-1 (2751/DEL/2008) has been prepared from tubers of Prureria tuberose, which has shown significant effect in preventing diabetic proteinuria and histological changes in kidney, along with significant rise in sensitivity of insulin in rats. Thus, it could be suggested that combination of BHUx and PTY-1, could be used as food supplement for prevention of diabetic complication like atherosclerosis and nephropathy.

Diabetes greets Atherosclerosis as IR lips LDLR An intracellular bonding.

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Introduction:

Diabetes mellitus (DM) is an emblem of natural model of atherosclerosis. DM and atherosclerosis are diseases accompanied by hypercholesterolemia. One of the reasons of hypercholesterolemia is...
dysfunctional LDL receptor (LDLR). Insulin has been found to modulate the expression and functional potency of LDLR. Signaling message from insulin to intracellular component is relayed through insulin receptor (IR). IR and insulin are aimed here to evaluate insulin mediated messages on LDLR expression and its functionality.

Methods:

Receptor expressions were checked by Immunocytochemistry/ western-blota / PCR. LDL uptake was measured by dil-LDL. Immunoprecipitation, confocal-microscopy & EM were done to see receptor association. siRNA was used to knock down LDLR expression.

Results:

Insulin stimulates both LDLR and IR expressions. Insulin also enhances functional activity of LDLR. Lacking insulin or insulin mediated signal in a state like diabetes represses LDLR expression but, adds more to explain the functional disability of LDLR. LDLR and IR were found to be co-adhered in their cellular existence and needed insulin for their free activity. Presence of insulin was found to be important to keep these two receptors separated for their free activity.

Conclusion:

The impact between IR and LDLR on cell surface provides a new area to diagnose the chances of developing atherosclerosis in a Subject suffering from diabetes mellitus particularly from Type-1 variety.

Small dense LDL particles in relation to LDL oxidation in normolipidemic cad patients

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Introduction: Studies of the heterogeneity of LDL particles and their number have suggested that small dense LDL particles and their number are important components in the risk evaluation of coronary artery disease.

Methods: Present study was conducted on 422 coronary artery disease (CAD) patients and 300 age and sex matched normal subjects who served as controls. Informed consent was taken before taking their fasting blood samples. Student’s t test was used to assess the significance. All the subjects were screened for various biochemical investigations such as lipid profile, serum apoB, MDA-LDL levels and LDL apoB carbonyl content.
Results: 30% (n=128) of the patients were observed to have normal lipid levels as per ATPIII guidelines. However, serum apoB levels were significantly raised (p<0.001) in CAD patients (148±12.9mg/dl) even in normolipidemic (130±12.6mg/dl) as compared to normal subjects (108±12.6mg/dl). Raised serum apoB levels are an indicative of increased number of small dense LDL particles. This observation was supported from the fact that normolipidemic CAD patients had significantly raised (p<0.01) positive values of Log (TG/HDL-C) ratio as compared to healthy subjects. Log (TG/HDL-C) ratio has been taken as an index of LDL particle size. Such LDL particles are more prone to oxidation. Both MDA-LDL levels and LDL apoB carbonyl content were significantly high (p<0.01) in normolipidemic CAD patients as compared to healthy subjects.

Conclusions: It may be concluded that evaluation of small dense LDL particles provides useful information of CAD risk even in normolipidemics.

Key words: normolipidemic, small dense LDL, apoB, LDL oxidation, CAD

Comparison of the various lipid ratios for coronary artery disease risk assessment in atherosclerosis-prone North Indian patients with acute myocardial infarction

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Objectives:

Coronary artery disease (CAD) is rapidly assuming epidemic proportions in developing countries including India. A plethora of lipid ratios, lipid indices and other calculated parameters such as atherogenic index of plasma (AIP) and non-HDL cholesterol have been evaluated recently by various researchers as tentative indicators of atherogenic load. We undertook the following study to assess the incremental utility of the various lipid ratios and indices as markers of CAD-risk in atherosclerosis-prone North Indian patients of acute myocardial infarction (AMI).

Design and Methods:

Study group comprised of 100 clinically assessed patients of AMI, diagnosed on electrocardiographic and biochemical criteria and 100 age and sex matched healthy controls. We evaluated serum total cholesterol(TC), high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), non-HDL cholesterol (non-HDL), lipid ratios (TC:HDL, LDL:HDL, triglyceride: HDL and non-HDL/HDL) and atherogenic index of plasma (AIP=log TG/HDL) in the study population. Lipid parameters were estimated
using standard methods. The various lipid ratios and lipid indices were calculated using standard formulae.

**Results:**

In our study, non-HDL/HDL emerged as the best performer among the various parameters assessed, with an area under the curve of 0.897 and an odds ratio of 12.3. Other parameters that performed well include non-HDL cholesterol and TC/HDL with area under curves of 0.834 and 0.812 respectively.

**Conclusion:**

Measurement of these indices established non-HDL/HDL as the best CAD risk determinant in the CAD-prone North Indian patients with AMI in our study, aiding in the risk stratification of the CAD patients in a great way. This insight into the clinical utility will prove highly beneficial for utilizing these ratios for diagnostic and prognostic purposes, besides the routine lipid profile.

Anti-Thrombotic role of Nano Silver

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**Introduction:** Atherosclerosis and thrombotic disorders have emerged as serious threat to our society. Platelet over activity can lead to thrombotic situations. Since anticoagulant and thrombolytic treatment strategies are usually associated with serious bleeding complications, the focus has now shifted to regulating and maintaining platelets in an inactive state.

Silver nanoparticles, through their interaction with various proteins have been shown to affect cell signaling mechanisms. We prospectively evaluated Silver nanoparticles for their Anti-Platelet Effects.

**Methods:** Platelets, isolated from anti-coagulated human whole blood sample from fifty healthy donors, were suspended in physiological buffer and each sample was divided into four tubes. In three of them 0.05, 0.5 and 5μM concentrations of Silver nanoparticles were added, fourth tube served as control.

Thrombin, ADP and collagen induced platelet aggregation, Platelet adhesion on immobilized fibrinogen matrices, integrin mediated cell signaling events and associated cytoskeletal changes, intra-cellular calcium levels and fibrin clot retraction were studied in all the four samples.

**Results:** In the present study we show that nanosilver has an innate antiplatelet property without conferring any lytic effect on them and effectively prevents integrin-mediated platelet responses in a concentration-dependent manner.
**Conclusion:** Silver nanoparticles appear to inhibit integrin mediated platelet responses. It has the potential for maintaining a lower activation state of platelets, decreasing platelet aggregation and their adhesion to Fibrin clot. Thus we conclude that Silver nanoparticles-Induce Anti-Platelet Effects and following appropriate trials may find a place among anti-platelet agents.

**Studies on adiponectin and proinflammatory cytokines levels in relation to the metabolic syndrome (obesity and type 2 diabetes mellitus).**

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**Introduction:** Obesity and Type 2 diabetes are the potent risk factors for the development of metabolic syndrome and coronary artery diseases and its prevalence is growing rapidly in India. Chronic inflammation may also be linked to it. Therefore measurement of adiponectin and proinflammatory cytokines may serve as important biomarkers for its immediate diagnosis.

**Methods:** The present study comprises of 88 subjects of age 30-60 years of either sexes which included group 1-22, obese diabetic patients (OD), Group 2-22, non obese diabetic (NOD), Group 3-22, obese non diabetic (ONGT) and group 4-22 non obese, non diabetic (Control). The fasting blood samples were analyzed for glycosylated hemoglobin, liver function test and serum lipids using standard methods. Serum insulin, hs CRP, IL-6 and adiponectin by ELISA method using standard kits.

**Results:** The value of serum adiponectin was significantly lower in both the obese Group 1 and Group 3 as compared to Group 2 and 4 (P<0.001) serum hs CRP and IL-6 levels were significantly higher in group 1, 2 and 3 as compared to group 4. Serum cholesterol and TG levels were significantly higher in group 1 as compared to other groups (P<0.001). A significant negative correlation was seen between adiponectin and cytokines hs CRP and IL-6. A significant positive correlation was seen between hs CRP and IL-6 levels.

**Conclusion:** This study has improved our understanding of the pathophysiological link between obesity, insulin resistance and associated inflammatory conditions thus measurement of serum adiponectin can be an asset as potent Biomarker of metabolic syndrome and coronary artery disease.
Effect of Aloe vera on doxorubicin-induced cardiotoxicity in rats

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Introduction: Doxorubicin (DOX) is a chemotherapeutic agent used effectively in the treatment of several malignancies. The major limiting factor associated with DOX treatment is cardiotoxicity caused due to the generation of oxygen free radicals. This study was undertaken to determine whether DOX-induced cardiotoxicity could be prevented by the natural plant product Aloe vera leaf gel extract.

Methods: Wistar albino male rats were assigned randomly to 12 groups viz. normal control, vehicle control, Aloe vera (100 mg/kg), Aloe vera (200 mg/kg), vitamin E, DOX-treated group, Aloe vera (100 mg/kg)+DOX, Aloe vera (200 mg/kg)+DOX, vitamin E+DOX, DOX+ Aloe vera (100 mg/kg), DOX+Aloe vera (200 mg/kg), and DOX+vitamin E. Following completion of the drug treatment, blood samples were analyzed to determine malondialdehyde (MDA), lactate dehydrogenase (LDH), creatine kinase, superoxide dismutase (SOD), and catalase (CAT).

Results: DOX induced cardiotoxicity in all the animals as evident from increase in all cardiac and oxidative stress parameters as compared to control. Aloe vera in doses of 100 and 200 mg/kg dose dependently attenuated the levels of all the parameters, in both pre- and post- DOX treated animals.

Conclusion: The positive effects of Aloe vera on the prevention of DXR-induced cardiotoxicity could be clearly seen. However, the administration of these natural plant products over longer periods may show more definite results.

Metabolic parameters, adiponectin and C-Reactive Protein in South Asian Women

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Background: The incidence of cardiovascular disease in South Asian Women is increasing both in the native and the migrant population. Altered cultural behaviour may be a reason for the altered risk profiles.
Methods: Fifty healthy Indian women (average age 39 yrs) (Group I) were randomly studied at the Hyperlipidemia Clinic, SGRH, Delhi. Their baseline characteristics and metabolic parameters included weight, lipids, glycosylated Hb and serum C Reactive Protein (Hs CRP). Adiponectin was assayed in 21 cases. A group of 123 healthy women (average age 31 years) recently migrated to the US from South Asia were studied by the Cardiology Division, Emory University. Baseline characteristics similar to their Indian counterparts were obtained at their time of arrival (Group II) and then 3 years later (Group III). Characteristics of the Indian Women (Delhi) (Group I) and South Asian migrated women (Group II) were also compared.

Results: Interesting features were observed between the US based S Asian women (Group II) and Indian Women (Delhi) based (Group I). HsCRP was significantly increased in Group II (p<0.001) in comparison with (Group I). Adiponectin (Group I) was significantly lower than those migrated to the US (Group II) (p<0.15). HDL also was found to be significantly lower between the two groups (p=0.004). In the S. Asian US based population an increase in LDL-Cholesterol was observed from (Group II, 103.8+18.8 mg/dl to Group III 109.1+12.2 mg/dl) (p=0.016). An increase (p=0.002) was observed in HbA1c levels in this otherwise healthy population over 3 years, p=0.002). A 7% reduction in serum adiponectin was also noted between Group II and Group III.

Conclusion: Various deranged parameters point to cardiac risk in both Indian and US based S. Asian women. This population needs to be identified at a younger age and treated aggressively.

Effect of Smoking on Metalloproteinase activity in Patients with Acute Myocardial Infarction

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Introduction: Many risk factors are involved in the course and pathogenesis of Acute Myocardial Infarction (AMI). Smoking can significantly increase the AMI mortality and morbidity. Matrix metalloproteinases (MMPs), a class of Zn containing enzymes, are involved in the erosion of the fibrous cap and rupture of the plaque which leads to AMI. The present study was aimed to evaluate the activity of two MMPs, MMP2 and MMP9 in AMI patients, with and without the habit of smoking to find out whether smoking could increase the activity of MMPs in AMI patients.

Methods: The blood samples from AMI patients and sex and age matched control subjects with and without the habit of smoking were analysed for MMP2 and MMP9 by sandwich enzyme immuno assay and the values were noted and compared.
Results: Both MMP2 and MMP9 were found to be significantly elevated in all AMI patients when compared to the normal controls subjects irrespective of the habit of smoking. However MMP9 showed a significant elevation when compared to MMP2 in patients with the habit of smoking.

Conclusion: The results of the present study shows increased concentration of both MMPs in AMI patients. However, concentration of MMP9 was found to be more in patients with the habit of smoking when compared to MMP2, indicating that smoking can increase the activity of MMP9 in these patients. Hence apart from producing the free radicals, the smoke can increase the activities of matrix degrading enzymes which in turn contribute to the vulnerability of plaque.

Study of Adiponectin and Ferritin in Healthy Adult population in Relation to Insulin Resistance

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Introduction: Insulin resistance and compensatory hyperinsulinemia underlie the clustering of metabolic disturbances and has an important risk factor for cardiovascular disease. Obesity has proven to be an independent risk factor for Coronary Artery Disease (CAD) in both genders. Adiponectin produced by adipose tissue exhibits various anti-inflammatory, antiatherogenic properties and prevents insulin resistance.

Material & Methods: The study was carried out in 80 healthy individuals (46 males and 34 females) in age group of 19—60 years after obtaining their consent. Fasting serum insulin, adiponectin and ferritin levels were measured by sandwich ELISA technique. Statistical analysis was performed by using SPSS software version-12.

Results & Discussion: We found 3 subjects (1 male and 2 female) with BMI>30kg/m² and 16 subjects (9 male and 7 female) with BMI>25kg/m². The mean insulin and adiponectin levels were high in females (6.38 µU/ml & 9.19 µg/ml) compared to males (6.38 µU/ml & 15.29 µg/ml) whereas ferritin levels were low in females (41.65 ng/ml) compared to males (99.22 ng/ml) respectively. Statistically significant inverse correlation (p<0.01) was found between adiponectin and WHR. Adiponectin was found to be directly correlated with HDL-C (r= +0.27, p<0.05) whereas Non-HDL-C and triglyceride level have shown insignificant inverse correlation. Ferritin correlates directly with WHR (r= +0.42, p<0.01) and WC(r= +0.30, p<0.01).

Conclusion: These observations suggest that adiponectin levels correlate inversely with obesity and serve its antiatherogenic lipid profile action whereas ferritin correlates directly with obesity. Thus, it suggests that adiponectin and ferritin may be a missing link in the etiopathogenesis of insulin resistance.
Are Leptin and Insulin a risk factor for atherosclerosis? A pilot study in North Indian population.

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Introduction: Leptin, a 167-amino acid peptide hormone produced by white adipose tissue, is primarily involved in the regulation of food intake and energy expenditure. Leptin receptors are expressed in many tissues including the cardiovascular system and its concentration is proportional to body adiposity and is markedly increased in obese individuals. Leptin is also linked to insulin resistance and the progression of insulin resistance parallels endothelial dysfunction related to atherosclerosis leading to cardiovascular disease and its complications.

Material and method: A pilot study was conducted with 80 healthy subjects who were non diabetic, non hypertensive and having no family history of hypertension, the aim was to evaluate the correlation of leptin levels with cardiovascular disease in healthy north Indian adult population. Leptin was estimated by human ELISA commercial kit. Serum insulin was estimated by sandwich ELISA method.

Result: In our study, Leptin correlated significantly with BMI (p-value of 0.0000), WC (p-value=0.007), and HC (p-value=0.000). Leptin showed significant positive correlation with fasting insulin (p-value 0.002), post prandial insulin (p-value=0.000) and HOMA –IR (p-value=0.002). Our study shows significant positive correlation of leptin with triglycerides (p-value=0.038), strong negative correlation with HDL-cholesterol (p-value=0.017).

Conclusion: Serum concentration of leptin was associated with central body fat distribution (central obesity) and insulin resistance. The clustering of central obesity with insulin resistance account for the proatherosclerotic effects of adiposity which modulate atherosclerosis and are candidate risk factors for CVD.

Polymorphism in the regulatory sequence of PON1 gene and its association with the risk of Cardiovascular Diseases.

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Introduction: PON1 protein is polymorphic and the two important polymorphic forms are L55M and Q192R. In addition to the polymorphisms in the coding region, PON1 has six polymorphisms in
promoter region. They are -108(C/T), -126 (G/C), -162(G/A), -832 (G/A), -909 (G/C) and -1076 (A/G). Recently, polymorphisms in the promoter region were found to be strongly associated with paraoxonase activity, with the polymorphism -108 having the greatest impact followed by PON1 192, PON1 55, PON1 -832, PON -162 and PON1-909. High PON activity was found with allele GG at -1074 position.

Methods: Since HDL-PON1 association is through the N-terminal hydrophobic peptide of PON1, in this study we wanted to investigate possible polymorphisms in the promoter region and in the first exon which would affect the amount of PON associated with HDL. 270 individuals were screened for the PON1 activity and the DNA of the individuals was screened for polymorphism from -1246 to +203 of PON1 gene with total sequence length of 1449 basepairs.

Results: We report the presence of 9 polymorphisms in the promoter region, with 3 novel polymorphisms, but none in the first exon of PON1. Out of three novel polymorphisms, two of them -725 (A/G) and -283 (C/T) are present in 5’ flanking region and -165 (G/C) is present in 5’ untranslated region. PON activity in these individuals ranged from 1527 to 106565 u/l. However the PON activity did not correlate with any of the polymorphisms except for novel mutation -725 A/G. The mutation -832 G/A is having significant association with CVD.

Conclusion: Our results suggest that PON variation in South Indian population may be independent of promoter polymorphism. The association between PON1 activity and the risk of CVD is controversial. Some reports state that PON1 protein levels are more important than the activity. Moreover HDL association of PON1 was essential for cardioprotection. It is possible that there may be variation in the secondary structure of the N-terminal peptide of PON1 leading to its abnormal association with HDL.

Influence of Withania somnifera on inflammatory and renal markers in experimental nephrotoxic rats

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In the present study, we investigated the protective effect of Withania somnifera root powder (an indigenous medicinal herb used in ayurvedic traditional systems for over 3000 years in India) on inflammatory markers [inducible nitric oxide synthase (iNOS) and transforming growth factor-beta (TGF-β)] by immunohistochemistry, renal [kidney injury molecule-(KIM)] and inflammatory markers [tumor necrosis factor alpha (TNF-α), nuclear transcription factor-κB (NF-κB), and nuclear factor E2-related factor 2 (Nrf2)] by western blotting; we have also investigated the mRNA expression of kallikrein, osteopontin, lipocalin 2 and clusterin by RT PCR on gentamycin (GEN)-induced nephrotoxic and W. somnifera treated rats. The root powder of W. somnifera (500mg/kg b.wt) was administered orally to
rats for 14 days and on 15th day, GEN (100mg/kg b.wt) together with W. somnifera were administered till the experimental duration of 22 days. In kidney tissues, iNOS and TGF-β showed positive staining, whereas KIM, TNF-α, NF-κB, osteopontin, lipocalin 2 and clusterin showed increased expression while Nrf2 and kallikrein level showed decreased expression in GEN treated rats. In contrast, rats treated with GEN and W. somnifera showed decrease in the expression of iNOS and TGF-β showed diminished staining, whereas KIM, TNF-α, NF-κB, osteopontin, lipocalin 2 and clusterin showed decreased expressions while Nrf2 and kallikrein expression was restored to near normal indicating the beneficial effect of W. somnifera in maintaining the structural integrity of the renal cells and by modulating the oxidative insult.

Role of tobacco cessation clinic at tertiary teaching centre and WHO’s MPOWER policies

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Background: More than 50% of patients continue to smoke despite multiple co morbidities and can be helped by providing counseling and pharmacotherapy in dedicated tobacco cessation clinics (TCC) by implementation of WHO’s MPOWER package which include monitoring tobacco use, protecting people from tobacco use, offering help to quit, and warning about the its dangers.

Objectives: To educate people regarding the harmful effects of tobacco consumption, screen them for cardiovascular and pulmonary risk factors and continue reinforcement of cessation.

Materials & Methods: Following a public awareness campaign, detail history regarding tobacco habit and cardiovascular and pulmonary assessment was made on prestructured proforma. Workup included carotid intima media thickness (CIMT), spirometry, ECG, fasting lipid, blood sugar estimation.

Results: 208 subjects were registered during Jun ‘08 to Jun’10. Most were (61%) young males (88.4%) (mean age 38.59 yrs). 42.7% were beedi or cigarette smokers, 41.8 % were taking oral tobacco/ gutkhas/ pan masala, and 15.3% were taking both beedi/cigarette and smokeless tobacco. 26.9 % were taking concurrent alcohol. On workup, 30.9 % were centrally obese, 30.7% had family history of cardiovascular allied disorders. 13.9 % were hypertensive, 4.3% were diabetics, and 89.5 % were dyslipidemic. Mean CIMT was 0.058 cms with plaque in 9.6% patients. Mean age of initiation of tobacco consumption was 21.7 years. Spirometry showed 26.7% had obstructive, 12.5% restrictive and 7.6% as mixed pattern of airway disease.

Conclusion: Use of tobacco is associated with asymptomatic cardiovascular and pulmonary morbidities. They could be helped by dedicated TCCs.

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INTRODUCTION: Ischemic heart disease (IHD) is the end result of atherosclerosis of coronary vessels. Despite having less prevalence of traditional risk factors, the disease manifests a decade earlier as compared to west which suggests a possible role of genes. In our study, we tried to evaluate the role of iNOS gene C150T, single nucleotide polymorphism, leading to amino acid substitution Ser608Leu in exon 16, in stable ischemic heart disease in north Indians.

METHODS: A case-control study, enrolling 50 documented stable ischemic heart disease patients (age≥35 years), attending medicine OPD of LHMC and SSKH and GB Panth hospital, New Delhi and 50 age & sex matched healthy volunteers with no known risk factors for IHD was conducted during May 2009-Apr 2010. Detailed history was obtained and examination done after written informed consent. PCR-RFLP was done using Tsp509I restriction enzyme to identify the polymorphism. Nitric oxide levels were measured by modified Griess reaction (Mathew et al. 1996). Statistical analysis was done using SPSS version 18.

RESULTS: The frequency of CT genotype (mutant type) was higher in cases than controls (30% vs 24%) whereas, CC genotype (wild type) was more frequent in control group than cases (76% vs 70%). The odd’s ratio and 95% CI of CT genotype was 1.36(0.56-3.3) and of CC genotype was 0.74(0.30-1.80) for IHD. The frequency of the T allele was higher in cases compared to controls (19.5% vs 12%). Nitric oxide levels were also elevated in cases with T allele.

CONCLUSION: The iNOS C150T polymorphism by affecting nitric oxide levels may have a role in etiopathogenesis of IHD. Though, association needs to be established with large scale studies.

Gene-diet interaction and risk of coronary artery disease

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Introduction: As gene polymorphisms have persisted much longer in the human race than the appearance of common disorders such as cardiovascular disease or type 2 diabetes mellitus, that have assumed epidemic proportions today, it appears that gene-disease association cannot be fully addressed without considering gene-environment interactions. Of the various environmental influences, food is one the most important due to the necessity for its daily consumption. Nutritional genomics addresses gene-diet interaction in health and disease. Nutritional status adversely affecting metabolic pathways such as folate metabolism demonstrate gene-diet interactions. The objective of this study was to evaluate folate gene-diet interactions.
Patients and Methods: A case-control study consisting of 252 diagnosed cases of coronary artery disease (CAD) and 252 age- and gender-matched asymptomatic controls were enrolled. The DNA polymorphisms documented included i) MTHFR 677C>T; ii) MTR 2756 A>G; iii) BHMT 742G>A SNPs; iv) 68-bp insertion in CBS gene; v) 6-bp deletion in TS gene and vi) 28-bp repeat polymorphism in TSER. Dietary assessment was made using a standard 24-hour recall coupled to food frequency questionnaire. Intake of folic acid, vitamins B6 and B12 were estimated.

Results: A positive gene-CAD association with minor allele was observed for i) MTHFR 677C>T in females (p=0.02); ii) TS gene 6-bp deletion polymorphism (p=0.03) and iii) BHMT 742G>A (p=0.04) in early onset CAD. The dietary intake of folic acid and vitamin B12 was significantly lower in females with CAD than in controls, suggesting a gene-diet interaction in case of MTHFR, representing the folate-dependent pathway of remethylation of homocysteine. The lowest quintile intake of folic acid, vitamins B12 and B6 occurred in a larger proportion of CAD patients than in controls (50% versus 37%; p=0.04), suggesting gene-diet interaction for BHMT representing the folate-independent pathway of remethylation.

Conclusions: Evaluation of gene-diet interaction in CAD or other clinical disorders might help in personalizing appropriate dietary intervention to prevent CAD.

Effect of L-Arginine on serum cholesterol levels during acute myocardial infarction

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Objective: Cholesterol plays vital role in maintaining cell membrane, manufacturing Vit.D, producing hormones and many more. But when the cholesterol level increases in the blood, it leads to dangerous consequences. Particularly cholesterol has generated great notoriety for its causative role in atherosclerosis, leading to myocardial infarction. The objective of this study is to evaluate the effect of L-arginine on serum lipid and cholesterol levels in the patients of acute myocardial infarction.

Methods: The study consisted of 70 AMI patients and 60 healthy individuals (serving as control) age 55-65 yrs. Serum levels of total cholesterol, HDL, LDL and Triglycerides were determined on day 1 and day 15 of L-arginine administration (oral dose 3g/day). The total cholesterol/HDL and the LDL/HDL ratio were calculated and compared.

Results: In control subjects from day 1 to day 15 of L-arginine supplementation, the (mean ± SE) total cholesterol (166.7± 2.22 vs 139.7± 2.53 mg/dl; p<0.01), LDL (99.4± 2.02 vs 80.8± 2.48 mg/dl; p<0.001)
and triglyceride (76.8± 1.73 vs 68.2± 2.49 mg/dl; p>0.05) decreased while HDL (51.2± 1.65 vs 55.1± 1.55; p<0.05) increased. The total cholesterol/HDL ratio was 3.25 on day 1 and 2.54 on day 15 (significant, p<0.001) in control group. The LDL/ HDL ratio was 1.94 on day 1 and 1.47 on day 15 (significant, p<0.01).

In AMI group from day 1 to day 15 of L-arginine supplementation, the (mean± SE) total cholesterol (213± 7.9 vs 154.3± 2.87 mg/dl; p<0.001), LDL (130.4± 1.55 vs 110.5± 2.73 mg/dl; p<0.001) and triglyceride (147.0± 2.27 vs 118.3± 14.65 mg/dl; p>0.05) decreased while HDL (31.7± 0.67 vs 41.7± 1.26 mg/dl; p<0.001) increased. Total cholesterol/HDL ratio on day 1 was 6.719 and 3.696 on day 15 (change significant) while the LDL/HDL ratio was 4.113 on day 1 and 2.647 on day 15 (p<0.001).

**Conclusion:** L-arginine is effective in controlling the serum cholesterol levels in AMI patients as well as in healthy subjects. Hence it could be used as an adjuvant therapy for AMI.

**Key words:** acute myocardial infarction; cholesterol; cholesterol ratios; coronary artery disease; coronary risk factor; triglycerides.

**Abbreviations:** HDL, high-density lipoprotein; LDL, low-density lipoprotein; MI, myocardial infarction

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**Significance of molecular markers of thrombophilia in young CAD patients**

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**Introduction:** Coronary artery disease (CAD) is the leading cause of death in developing and developed countries. Individuals with genetic predisposition to atherosclerosis have substantial risk for developing CAD, especially at early ages.

Thrombogenicity, the state of activation of coagulation cascade, the fibrinolytic system and various other biochemical factors are complex and interrelated biologic process that contributes to atherogenesis and clinical manifestation of atherosclerosis.

In the present study we have studied the association of factor V Leiden, Prothrombin gene polymorphism, MTHFR gene and TNFR2 gene mutation by PCR along with other biochemical parameters in young CAD patients

**Methods:** Thirty diagnosed patients with CAD of either sex under 40 years were included Thirty healthy age and sex matched control subjects without evidence of CAD formed the control group. Detailed history and clinical examination findings were recorded. Screening by PCR based technique was carried out along with lipid profile, screening coagulation tests, C-reactive protein and fibrinogen levels.
**Results:** The mean age (±SD) was 36.9±3.9 years in the patients. FVL, MTHFR and TNFR-2 gene mutation were seen in 9(30%) patients; among this mutation in combination was seen in 3(10%) patients. FVL was seen in 4(13.3%), MTHFR gene mutation in 3(10%) & TNFR-2 gene mutation in 5(16.6%) Prothrombin gene mutation was not seen in any of the subjects. Smoking was the most prevalent risk factor. There was a significant difference in the CRP>6 /CRP< 6 among the patients with TNFR2 mutation and among patient who were negative for the mutation. There was no significant difference in lipid profile, fibrinogen levels and CRP among the patients with mutation and patients without mutation.

**Conclusion:** The cases positive for these molecular markers along with other risk factors in the present study though being a small number of patients is strongly indicative of the association in causation of young CAD lacking conventional risk factors. Thus, there is a need to demonstrate or document these mutations in a larger group further based upon ethnicity and geographic distribution.
Poster Papers
Learning curve of Tobacco Habit in young- our experience at tobacco cessation clinic

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Background: The best way to control tobacco consumption is to understand the dynamics of its initiation and intervene at the initiating point.

Objectives: To elucidate the age at which this habit was acquired, the source from where they learnt this, type of tobacco used, and concomitant use of other substance abuse, if any in young.

Materials & method: We studied the profile of all subjects ≤ 35 years of age attending the tobacco cessation clinic (TCC) from May 2008 to June 2010. A structured tobacco questionnaire was filled and general examination done for all subjects.

Results: A total of 100 young subjects were registered comprising 92 males, 6 females and 2 transgenders. The mean age was 27.35 years, youngest being a 14 years old male. The mean age of initiation was 18.4 years, youngest being 6 years. 45% were consuming tobacco by 18-years of age. Most common form of tobacco use were gutkha (26%), oral tobacco (21%), cigarette smoking (16%), bidi smoking (15%); while 22% were polytobacco users. 28% were taking alcohol concurrently. The pattern of smoking in the family showed that 40% had both parents and siblings as smokers, 32% had parents alone and 5% had only siblings as smokers.

Conclusion: The presence of smokers in family members in 77% of subjects indicate that first lessons of tobacco habit is usually learnt at home in young. Smoking cessation programs should be complimented with prevention of initiation of tobacco consumption. Consumption of smokeless tobacco, presumably considered harmless, deserves special attention.

Influence of psychosocial factors on the clinical and biochemical parameters of Metabolic syndrome in Patna.

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Introduction: Metabolic syndrome, resulting from a complex interplay of genetic inflammatory and environmental factors is associated with increased cardiovascular morbidity and mortality. The objective of this study was to investigate the psychosocial risk factors associated with metabolic syndrome and its components in Patna, which has a distinctly different pattern of diet, lifestyle and culture.
Methods: 642 apparently healthy subjects were selected randomly from the OPDs of Patna Medical College & Hospital and from the local population. All the subjects were screened through a questionnaire based interview, anthropometric measurements and biochemical investigations. Cases were defined on the basis of the NCEP ATP III criteria. Prevalence of metabolic syndrome and its components were calculated in different groups divided on the basis of psychosocial factors and data was analyzed using SPSS-V16.

Results: 24.1% of the study population had metabolic syndrome. Females showed a slightly higher prevalence than males. Unlike the western countries, a higher prevalence was observed among those belonging to high socioeconomic group (p<0.05). Vegetarians surprisingly showed a high prevalence. The prevalence among sedentary subjects was significantly higher in comparison to active subjects (p=0.002).

Conclusions: The educated urban upper-middle class population of Patna had a higher risk of developing metabolic syndrome due to erratic dietary habits, sedentary lifestyle and increasing professional stress. Non working middle class women were the worst victims. The role of sociobiological translation in pathogenesis of metabolic syndrome cannot be overlooked and further research must be undertaken to emphasize on a holistic approach towards prevention and management of this worldwide epidemic.

Level of high-sensitivity C-reactive protein and interlukin-6 in patients with stable coronary artery disease

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Background: Inflammatory biomarker i.e high-sensitivity C-reactive protein (hsCRP) and interlukin-6 (IL-6) are independent predictor of future cardiovascular events and it predicts risk of incident hypertension.

Objectives: The aim of this study was to determine the serum levels of the circulating hsCRP and IL-6 in patients with stable Coronary Artery Disease (CAD).

Methods: This study was conducted in the Department of Biochemistry and Department of Medicine, Lady Hardinge Medical College, New Delhi. 50 individuals with stable CAD and 50 healthy, age and sex matched individuals were considered in this study. Overnight fasting blood samples were collected and analyzed for total cholesterol (TC), Triglycerides (TG), Low Density Lipoprotein (LDL), High Density Lipoprotein (HDL), hsCRP and IL-6 in patients with stable CAD.
Results: TC, TG and LDL levels were significantly higher (p<0.01) whereas HDL level was significantly lower (p<0.05) in stable CAD patients as compared to control. hsCRP and IL-6 levels were significantly higher (p<0.001) in patients with stable CAD as compared to control.

Conclusion: Patients with stable CAD have higher hsCRP and IL-6 levels. The ratio of HDL-cholesterol was more strongly associated with the risk of coronary artery disease than were the levels of inflammatory markers. IL-6 and hsCRP were still a significant contributor to the prediction of coronary artery disease.

Hypocholesterolemic effect of central stem of *Musa sapientum* Linn.

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The hypercholesterolemic effect of aqueous extract of central part of stem of *Musa sapientum* Linn. (AqMS) has been investigated in rats made hypercholesterolemic by feeding cholesterol. Rats were divided into four groups: Group I served as healthy control; groups II served as a vehicle control, groups III and IV were made hypercholesterolemic by feeding cholesterol suspended in soya oil at the dose of 100mg/kg/day for six weeks. Group IV received AqMS at a dose of 50mg/kg / day orally in addition to cholesterol. Cholesterol fed rats showed significant increase in serum total cholesterol, triacylglycerol, LDL+VLDL-cholesterol whereas HDL-cholesterol decreased significantly as compared to healthy controls (p<0.01). Vehicle treated group showed slight rise in cholesterol level and triacylglycerol. Aq. MS treated groups showed significant decrease in serum cholesterol, triacylglycerol and LDL+VLDL-cholesterol levels as compared to group IV (p<0.01) whereas HDL-cholesterol was significantly increased (p<0.05). Results show that the aqueous extract of central stem (AqMS) has significant hypercholesterolemic effects.

Evaluation of hypolipidemic and antidiabetic activity of germinated *Glycine max* seeds

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The International Diabetes Federation estimates that diabetes accounts for 6% of total global mortality, with 50% of diabetes-associated deaths being attributed to cardiovascular disease (CVD). Individuals with diabetes have twice the incidents of myocardial infarction (MI) as compared with the general population. Improved diagnosis and effective treatments have definitely helped in decreased mortality from CVD as well as diabetes during the past few decades. However, the major focus is moving towards the herbal
plants which are effective with minimum side effects. This study investigates the hypolipidemic and anti-diabetic potential of *Glycine max* seeds.

In our 21 day study, an aqueous extract of 12 hrs germinated *Glycine max* seeds was administered orally to STZ induced diabetic male wistar rats (160-200 g). Rats were divided into 4 groups (n=5) i.e. normal healthy, diabetic control, diabetic + Glibenclamide (600µg/kg b.w.) and diabetic + extract. Initially different doses of extract were given and optimum dose was selected as 200mg/kg b.w. Fasting blood samples were collected after each week and analyzed for blood glucose levels, lipid profile (total cholesterol, triglyceride, HDL-Cholesterol, LDL-cholesterol and VLDL-Cholesterol), Apolipoprotein B and ox LDL.

Oral administration of extract to experimental rats showed significant (p<0.01) improvement in blood glucose and lipid profile. Apo B, ox LDL along with atherogenic index was also improved when compared with diabetic control group.

Our study concludes that the aqueous extract of germinated *Glycine max* seeds have significant hypolipidemic and anti-diabetic activity.

**Effect of life style intervention on risk parameters in young Indians suffering CAD**

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**Background:** Coronary artery disease (CAD) in young (age<=35-yrs) is increasing in Indian subcontinent. It constitutes 11-14% of total CAD burden in this country. In the background of dual epidemic of communicable and non communicable diseases prevailing in India, the crucial issue is can we prevent the risk of CAD in young by appropriate health intervention?

**Materials & methods:** We conducted a case-control interventional study in young CAD subjects and collected data from first episode CAD in patients (age<=35 yrs) admitted in coronary care unit of the GTB Hospital and studied effect of life style intervention with the help of power point presentation and booklet on risk factor profile (smoking, hypertension, diabetes mellitus, dyslipidemia, obesity , sedentary life, dietary habit) and short term mortality at three and six months follow up in test and control groups.

**Results:** A total of 500 subjects diagnosed as acute coronary syndrome from Sept 2008 to Jun 2010 were enrolled for this study. About 10 %( 49) subjects were young (=35yrs). Majority of them were men 40(81.6%), belonging to low socio economic group 42(85.7%) and were smokers, 34(69.4%). We observed a significant reduction in smoking (p<0.008) and significant difference in total cholesterol [Median (IQR)=170(133-179) mg/dl to 131(87.25-171.5)mg/dl] p<(0.046)and fat intake [Median(IQR)=56.35(41.95-78.35) g/day to 42.97(28.93-65.28) g/day ] (p<0.048) in study groups after six months follow up, whereas
in control group didn't show these beneficial changes. During six months follow up one patient in study group who was a smoker and alcoholic both died.

**Conclusion**: The findings of this short study reveal that adopting by lifestyle changes CAD risk factors can be modified which may be beneficial for them in preventive future episodes of acute coronary syndrome.

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**Role of insulin resistance in patients with premature Coronary Artery Disease**

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**Introduction**: Insulin resistance is associated with a greater risk of atherosclerotic cardiovascular disease. Assessment of insulin resistance is difficult, therefore we compared homeostasis model assessment (HOMA) and glucose to insulin (G: I) ratio in patients suffering from newly diagnosed premature coronary artery disease.

**Methods**: Present study was undertaken in department of Biochemistry GB Pant Hospital, New Delhi, India. The study group comprised of 50 patients of premature CAD and 50 age and sex matched healthy controls. Serum samples of all the subjects were assayed for glucose, Insulin, lipid profile and ferritin. Homeostasis model of assessment (HOMA-IR), (G: I) and ferritin were employed as surrogate measures to assess the level of insulin resistance.

**Results**: Patients with premature CAD demonstrated insulin resistance as observed by the higher HOMA – IR (4.02±1.1 vs. 2.21 ±0.8; p< 0.01) and G: I ratio (11.2± 5.1 vs. 16.1 ± 7.3) as compared to the controls. Ferritin levels were also found to be significantly higher in cases as compared to controls (84.3 ± 39.8 vs. 55.7 ± 29.6  ng/ml) respectively.

**Conclusion**: Insulin resistance contributes to pathogenesis of atherosclerosis. Timely diagnosis and effective management of insulin resistance will help in reducing morbidity and mortality due to cardiovascular disease in Indian sub continent.

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**Effect of atorvastatin monotherapy & atorvastatin,raw garlic combination therapy on lipid profile in patients of diabetes mellitus type-2**


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Introduction - Diabetic dyslipidemia accounts for around 80 percent diabetic deaths due to cardiovascular complications. Garlic is widely promoted as a cholesterol lowering agent. We evaluated the effect of raw garlic on cholesterol levels in hypercholesterolemic adults in addition to Atorvastatin.

Methods - A comparative study on 44 patients aged have been conducted for a duration of 12 weeks in the Department of Pharmacology in collaboration with Department of Medicine, S.N medical college & hospitals, Agra. Group-A of 22 patients received 10gm Atorvastatin daily. Group-B of 22 patients received 5gm raw garlic and 10mg Atorvastatin daily.

To observe the effect on lipid profile Total cholesterol (mg/dl), HDL cholesterol (mg/dl), LDL cholesterol (mg/dl), Triglycerides (mg/dl) was done prior to the treatment and after 12 weeks. Patients were told to follow dietary habits strictly.

Results - After 12 weeks of therapy:

Total cholesterol decrease 26% in Group-A patients and 35% in Group-B patients.
HDL cholesterol increase 8.1% in Group-A patients and 8.3% in Group-B patients
LDL cholesterol decrease 36% in Group-A patients and 40% in Group-B patients
Triglycerides decrease 22% in Group-A patients and 34% in Group-B patients

Conclusion - Adding raw garlic to Atorvastatin have favourable effect on lipid profile. It decrease Triglycerides and Total cholesterol significantly, but effect on LDL cholesterol and HDL cholesterol were inconsistent. As this study is done only in few patients, further study are needed to confirm the benefit of raw garlic on lipid profile with Atorvastatin.

Effect of monosodium glutamate (MSG) on various lipid fractions and certain antioxidant enzymes in arterial tissue of alcoholic adult male mice.

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Introduction: The consumption of monosodium glutamate, a sodium salt of glutamic acid and alcohol are becoming a part of daily food especially in younger generation. There are many reports in literature that the age for the establishment of atherosclerosis has become 30 years in the present where it was about decade back. So, it is matter of great concern as the number of premature deaths due coronary heart disease is increasing alarmingly. Aim: In the present work we wanted to study the effect of MSG by evaluating the change in oxidative stress in arterial tissue of chronic alcoholic adult male mice’s.

Material & Methods monosodium glutamate was given orally to alcohol consumed (30% for 37 days) adult male mice at dose levels of 4 and 8mg/g. b. wt. for consecutive 7 days and its effect was observed on
lipid peroxidation and antioxidant initiating & scavenging enzymes along with lipid profile in the arterial tissue of adult male mice’s

**Results:** a significant increase was observed in the levels of lipid fractions, lipid peroxidation, xanthine oxidase significantly increased whereas the levels of superoxide dismutase, catalase, glutathione and its metabolizing enzymes like glutathione peroxidase & glutathione reductase significantly decreased in the arterial tissue of all the study groups.

**Conclusion:** The ingestion of MSG to chronic alcoholic animals had no beneficial effect and thereby, could act as an additional factor for the initiation of atherosclerosis.

**Key Words:** Monosodium glutamate, alcohol, lipid peroxidation (LPO), Oxidative Stress and Atherosclerosis.

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**Protective effect of Active Compound Isolated from *Cassia auriculata* L. Leaves on lipid peroxidation and endothelial dysfunction**

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Diabetes mellitus is very often associated with dyslipidemia, increased oxidative stress and endothelial dysfunction that could develop atherosclerosis and consequently cardiovascular diseases. Medicinal plants with reputed traditional use to treat diabetes and cardiovascular diseases might provide valuable drugs. Therefore, the present study was undertaken to evaluate anti-atherosclerotic potential of active compound isolated from *Cassia auriculata* L. leaves in streptozotocin (STZ)-induced diabetic rats. The compound isolated was elucidated as a coumarin derivative on the basis of NMR spectral analysis and designated as CA₁₀₀. Diabetic rats were orally administered with CA₁₀₀ at a dose of 20 mg/kg body weight for 15 days. The supplementation of CA₁₀₀ exhibited significant antihyperglycemic activity along with significant reversal in the altered serum lipid profile. Lipid peroxidation measured as malondialdehyde (MDA) in serum was found to be suppressed in CA₁₀₀-fed diabetic rats. The significant reduction in the serum levels of oxidized low-density lipoprotein (OxLDL), soluble vascular cell adhesion molecule (sVCAM-1) and plasma fibrinogen with a concomitant elevation in serum nitric oxide (NO) level was observed in diabetic rats following treatment with CA₁₀₀. Histopathological examination of heart myocardium of CA₁₀₀-treated diabetic rats revealed reversal of fatty steatosis towards normal. These results suggest that CA₁₀₀ plays anti-atherosclerotic role in the diabetic state and it indicates towards the notion that CA₁₀₀ may help to prevent the progression of cardiovascular diseases.
Pulmonary function and oxidative stress in workers exposed to styrene in plastic factory

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Styrene is a volatile organic compound used in factories for synthesis of plastic products. The pneumotoxicity of styrene in experimental animals is known. The aim of the present study was to study the effect of styrene on lung function and oxidative stress in occupationally exposed workers in plastic factory. Thirty four male workers, between 18-40 yrs of age exposed to styrene for atleast 8 hours a day for more than a year were studied, while 30 age and sex matched healthy subjects not exposed to styrene served as controls. Assessment of lung functions showed a statistically significant reduction (p<0.05) in most of the lung volumes, capacities (FVC, FEV1, VC, ERV, IRV, IC) and flow rates (PEFR, MEF75 %, MVV) in the study group (workers) as compared to controls. It shows that styrene inhalation by workers leads to lung damage reflected in the lung function parameters.

Ferritin as a marker of oxidative stress in coronary artery disease.

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Background- Coronary artery disease (CAD) is the leading cause of death in India. It has been projected that by the year 2010, 60% of the world’s patients with heart disease will be in India. Many studies suggest a link between iron storage and development of coronary artery disease. Iron donates electron to promote formation of reactive oxygen species via Fenton reaction and causes oxidation of low-density lipoprotein, a trigger for development of atherosclerotic CAD.

Methods-This study was conducted in Department of Biochemistry in collaboration with Department of Cardiology, G. B. Pant Hospital, New Delhi, India. Patients were sub-classified in four groups, according to level of stenosis in coronary vessels with 50 patients in each group. Serum ferritin was assayed using ELISA based on Sandwich Principle. Statistical analysis was carried out using SPSS for windows 12.0 software.

Result- Serum ferritin levels were found to increase as we moved from normal coronary angiography to increased arterial stenotic state (55.0±19.0 ng/ml in G0 to 317.7±87.3 ng/ml in G4) (p<0.0001).
Conclusion- Oxidants as reactive oxygen species release iron from ferritin either directly or through heme oxygenase. This accelerates atherosclerosis via stimulation of LDL oxidation.

Susceptibility of Lipoprotein to oxidation: A comparative study of South Indians and Iranians

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Lipoproteins can undergo different types of modifications to different extent in vitro and in vivo. Oxidative modification is one such modification which changes the physico-chemical properties of the lipoproteins. Oxidized LDL in the arterial wall can lead to several pro-inflammatory reactions leading to atherosclerosis.

Several studies have tried to establish the beneficial effects of antioxidant in preventing lipoprotein oxidation. It is likely that there is an interplay between water soluble and lipid soluble antioxidants and the antioxidant enzymes. However little is known about the natural antioxidants that are present in the blood and their role in preventing oxidation.

In this study we have compared the antioxidant capacity of Iranian and Indian serum samples and their ability to prevent oxidation of lipoproteins in vitro. we have taken 50 serum samples from individuals who ages range from 24 years to 83 years, both males (56%) and females (44%). The whole serum was subjected to Cu⁺⁺ catalyzed oxidation in the presence of 5µM Cu⁺⁺ ions. The generation of oxidized lipids was monitored by formation of conjugated dienes at 234nm for up to 90min. The serum samples were also oxidized by Benzoyl peroxide.

Our results show that though the Iranian samples had higher HDL, their PON activity was about 25% of that of the Indian samples. The antioxidant capacity and reduced glutathione in the two samples was not significantly different. However the susceptibility of the serum to oxidation by either Cu⁺⁺ ions or Benzoyl peroxide was higher in the Indian samples compared with the Iranian samples.

Our results suggest that although the serum PON activity of Indian is higher, it may not protect lipoprotein oxidation.

Lipid Lowering by Phytochemicals: Inhibition of Malic enzyme by an extract of Artocarpus species

Shirin Tarbiat, Avila DSilva and Cletus J.M.DSouza
Dyslipidemia characterized by elevated serum cholesterol, elevated triglycerides and decreased HDL, is the key trigger factor for atherosclerosis. Three groups of drugs are used to treat this atherogenic triad, namely statins, fibrates and niacin. Statins and fibrates lower LDL thereby reducing cholesterol and triglycerides. Niacin is the only known drug to increase HDL. Since all these groups of drugs have side effects, phytochemicals are a promising group of molecules as alternate therapy.

Genus Artocarpus has more than 50 species of which jackfruit and bread fruit are well known. One of the species of Artocarpus grows as a wild tree in southern India. Its fruit is traditionally used as souring agent in many preparations and is commonly believed to lower lipids.

A methanolic extract of the dried fruit was prepared and tested for its lipid lowering effect. The methanolic extract was dried weighed and redissolved in ethanol. It was fed orally once daily at 1 mg/kg body weight for 4 weeks. At the end of each week, serum cholesterol and triglyceride were assayed. Malic enzyme was assayed in the liver homogenate.

In 4 weeks the serum cholesterol was reduced by 20% and triglycerides by 40%. There was a dose dependent inhibition of Malic enzyme in the liver.

Our results suggest that the lipid lowering effect of the Artocarpus may be due to inhibition of fatty acid biosynthesis.

Diabetes mellitus: Ancient food in modern life

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Since ancient times human society has been struggling for survival from unkind natural drought and famine. Its collective efforts however, led to the dawn of modern era through industrial revolution. Modernization undeniably improved the living standard of humans; it also surfaced several chronic diseases like type 2 diabetes mellitus and cardiovascular disorders. These metabolic disorders are being explained as the struggle of ancient metabolism in the modern affluent world, with the help of stipulations like thrifty genotype, phenotype, and metabolism carried forward by the humans through evolution.

In the race of modernization, India is facing double burden of malnutrition, along with epidemics of type 2 diabetes mellitus and cardiovascular disorders. Ancient Bharateeya medical texts describe in detail the causes; course and therapeutics for type 2 diabetes mellitus (Prameha / Madhumeha) and obesity (Medoroga).
In the course of our search for antidiabetic properties in Indian food, we investigated some food grains used in India since ancient times described beneficial in the management of diabetes mellitus and obesity. Among eight food-grains studied, extract of Yava (Hordeum vulgare Linn.), Sali (Oryza sativa Linn.), and Chanak (Cicer arietinum Linn.) displayed potent antihyperglycemic activity with varying degrees of free-radical scavenging, and antioxidative properties.

Above observations deserve detail scientific study in order to explore full potential of these food grains in mitigation and/or reversal of lifestyle related disorders like diabetes and obesity, and may fill the glaring gap of absence of research on lifestyle intervention to prevent or reverse these disorders.

Distribution of LDL Particle subclasses and LDL particle size in Indian population

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Introduction: Coronary artery disease (CAD) is one of the leading causes of morbidity and mortality in India. Attempts to determine the risk of heart attack and stroke based on a single criterion such as total cholesterol levels in different population groups have had limited success. For example, a follow-up to the Framingham study found that nearly half of the cases of coronary disease occurred in people with normal cholesterol levels. Hence, we studied the distribution pattern of Low-density lipoproteins (LDL) particle subclasses and their particle size in Indian population.

Material & Method: LDL subfraction profile was analysed by polyacrylamide gel electrophoresis (PAGE) using the Lipoprint system (Quantimetrix, USA) in 100 subjects.

Results: Small, dense LDL subfractions (4-7, nontype A) which are generally considered more atherogenic, were found to be statistically significant in males and in subjects with normal total cholesterol (p<0.05).

Conclusion: The study shows that LDL subfraction profile may be deranged in male subjects and in subjects with normal total cholesterol. This may have significant implications for the identification and management of high risk subjects. It will also help in selection of antihypertensive and lipid lowering treatments in such patients.

Effect of antibiotics on PON1 activity: Modulators or Substrates?
**Paraoxonase1 (PON1) is a HDL-associated enzyme found in the blood of animals. It is an antioxidant molecule with a variety of substrate specificities. In humans, the activity of this enzyme has been correlated with antiatherogenic property.**

One of the most common therapeutic molecules widely used are antibiotics. They are distributed to the different tissues by circulation in blood. Through absorption from the GI tract or through injection, the concentration of the antibiotics tends to be high in the blood.

In this study we have investigated the role of antibiotics in activation or inhibition of serum paraoxonase activity in vitro. Tetracycline, Chloramphenicol, Ampicillin, Gentamicin, Spectinomycin, Penicillin and Kanamycin were mixed with serum in increasing concentrations prior to determining the PON1 activity in the serum.

Tetracyclin, Chloramphenicol and Ampicillin were inhibitory to PON whereas Gentamicin, Spectinomycin, Kanamycin and Penicillin G had no effect on the activity.

Penicillin G was tested by TLC and spectroscopic techniques to see whether the PON had acted on it. From the NMR and IR spectra, it appears that the β-lactam ring of penicillin was cleaved.

Our results suggest that while doing an assay of serum PON1, the presence of endogenous antibiotic can be a confounding factor, particularly when correlation studies are made.

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**Diesel Exhaust causes protein carbonylation in vitro**

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The introduction of carbonyl groups into proteins can occur by products of Reactive Oxygen Species which can oxidize the side chains of amino acids or cleave the polypeptide oxidatively. Protein carbonyls can also be formed by secondary reactions of nucleophytic side chains of amino acids with glucose and carbonyl groups generated from glucose like glyoxal, methyl glyoxal and glucosone. Protein carbonyls are identified in diseases like diabetes and cardio vascular diseases.

Amino acids, proteins and serum were subjected to carbonylation reaction using acetic anhydride and acetyl chloride. The protein carbonyls were qualitatively identified through chromatographic techniques and quantitatively by reaction with DNPH. Diesel exhaust was condensed into water. The condensate was concentrated and filtered to remove particulate matter. The nanoparticles were treated with amino acids, proteins and serum. Paraoxonase activity of serum was measured before and after treatment with acetic anhydride or diesel exhaust.
Diesel exhaust was able to carbonylate amino acids, proteins and serum. Carbonylation of serum caused a dose dependent loss of serum Paraoxonase activity.

One of the risk factors of CVD is believed to be exposure to diesel exhaust, where the carbon nanoparticles can modify serum proteins, particularly the cardio protective molecules like HDL and HDL-associated enzymes. In this study we show that diesel exhaust can cause protein carbonylation in vitro.

Role of intergenotypic variation of nitric oxide and inflammatory markers in preeclampsia- pilot study in north Indian population
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Introduction: Cytokines appeared to contribute to the development of pathological condition and eNOS gene polymorphism may affect cytokine production. The aim of this study was to evaluate cytokines pattern in preeclampsia and whether there is any relationship between gene and cytokines production and cytokine with disease severity or not.

Method of study: This cross-sectional study included 300 women with preeclampsia and 200 healthy pregnant women. Their blood samples were analyzed for nitric oxide, inflammatory cytokines and eNOS gene polymorphism.

Results: Decreased NO and increased cytokines (Tumor Necrosis Factor-α, interleukin-2 and Interferon-γ) levels were found in preeclampsia (p<0.001). Significant differences were found in genotype/allele distribution between two groups. Significant negative correlation was seen between NO and cytokines levels (TNFα & INFγ) in preeclamptic group (p=0.001).

Conclusion: We concluded that preeclampsia is associated with decreased levels of nitric oxide and increased levels of circulating inflammatory cytokines due to SNP, pointing towards the role of endothelial and inflammatory components.

Keywords: Preeclampsia; Nitric Oxide; eNOS gene polymorphism; Inflammatory Cytokines
Hypolipidemic effect of aqueous extract of *Withania coagulans* in cholesterol fed hypercholesterolemic rats

Kirtikar Shukla, Piyush Dikshit, Rimi Shukla, Jasvinder K Gambhir

The hypolipidemic effect of aqueous extract of fruit of *WC* has been evaluated in cholesterol fed hypercholesterolemic rats. Rats were divided into three groups: Group I served as healthy control; groups II and III were made hypercholesterolemic by feeding cholesterol powder suspended in ground nut oil at the dose of 100mg/kg/bw/day for six weeks. Group III received cholesterol (100mg/kg bw) + aqWC at a dose of (250mg/kg bw/ day orally). Cholesterol fed rats (group II) showed significant increase in serum total cholesterol (TC), triacylglycerol (TAG), LDL+VLDL-cholesterol and ox-LDL whereas HDL was significantly decreased as compared to controls (group I) (p<0.01). Treatment with aqWC (group III) showed significant decrease in TC, TAG, LDL+VLDL-cholesterol and ox-LDL levels (p<0.01) whereas HDL was significantly increased (p<0.05) as compared to group II. Thus, these results show that the aqWC extract has significant hypocholestrolemic effects and brings about favorable changes in the lipid profile in cholesterol fed rats.

Hydrogen Peroxide - an inactivator and a substrate for serum Paraoxonase.

Austin Richard.S, Sindhu.S and Cletus JM D’Souza

Serum paraoxonase (PON) is a calcium-dependent esterase that is known to catalyse the hydrolysis of organophosphates, and is widely distributed among tissues such as liver, kidney, intestine, and also serum, where it is associated with HDL.

PON can offer protection against the toxicity of some organophosphates, but its physiological role is still not known; however, evidence exists for a protective effect of PON against oxidative damage. PON was suggested to contribute to the antioxidant protection conferred by HDL on LDL oxidation.

In present study we showed that PON having low level of peroxidase like activity by using hydrogen peroxide as substrate.

Increasing concentration of hydrogen peroxide was mixed with serum prior to determining its PON Activity using phenyl acetate as substrate. The lipid peroxides formed by the treatment of hydrogen peroxide were quantitatively estimated by thio-barbituric acid reaction.
With the increasing concentration of hydrogen peroxide the PON activity decreased. When the enzyme was allowed to remain in the presence of hydrogen peroxide for period up to 1 hour, the PON activity recovered. However when the initial concentration of hydrogen peroxide was high and the enzyme activity was completely destroyed, on incubation the PON activity did not recover. In a peroxidase assay with hydrogen peroxide as substrate, increasing enzyme concentration showed an increase in activity. This activity was completely abolished by EDTA.

Our results suggest the PON has peroxidase activity. Hence in the presence of hydrogen peroxide, the enzyme inactivated by oxidation may be recovered by the residual PON activity.

Familial xanthelasma with dyslipidemia – a clue to CAD in the young

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A 35 year old male, non-smoker, non-tobacco user, tea toaller, not a known case of hypertension or diabetes, embroidery worker by profession, presented with complaints of retrosternal discomfort, ‘ghabrahat’ and sweating for one hour. His father had died of acute coronary syndrome at 40 years of age. Clinical examination revealed evidence of extensive bilateral xanthelasma and central obesity (Fig.). His blood pressure was 112/76 mmHg on presentation. The ECG was suggestive of inferior wall ST elevation myocardial infarction (MI). His fasting blood sugar was 97 mg/dl and 2 hour postprandial blood sugar was 104 mg/dl, CRP >0.8 mg/l, total cholesterol 217 mg/dl, HDL-C 24 mg/dl and triglycerides 124 mg/dl. His carotid intima media thickness was normal. On detailed enquiry, his mother and younger brother also had evidence of xanthelasma without any subjective or ECG evidence of coronary artery disease (CAD). This case highlights the importance of familial xanthelasma as a cutaneous marker for CAD in the young, especially when associated with dyslipidemia. One must be wary of the tendency to dismiss familial xanthelasma as ‘just another family trait’ and look for underlying dyslipidemia and evidence of early onset CAD in these patients.

Beneficial Effect of Dietary Tocotrienols on Infection/Inflammation Induced Hepatic and Renal Lipid Peroxidation in Hamsters

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Introduction: Several epidemiological studies have documented an increased incidence of coronary artery disease in patients having chronic infections and inflammatory disorders. Infection/inflammation is accompanied by a systemic host response known as acute phase response (APR), which leads to the generation of plenty of free radicals that causes oxidative stress.

Material and Methods: In experimental animals (Syrian hamsters), infection and inflammation were induced by administration of endotoxin, lipopolysaccharide (LPS, acute systemic infection), zymosan (acute noninfectious systemic inflammation), and turpentine or croton oil (acute localized sterile inflammation). Tocomin (dietary tocotrienols, 10 mg) was fed to hamsters for 10 days before and 12 h after LPS or 24 h after turpentine or zymosan injection, respectively. The antioxidant impact of Tocomin in the above three distinct models was investigated.

Results: As part of host response to infection/inflammation, hepatic lipid peroxidation products, namely, conjugated diene, lipid hydroperoxides and malondialdehyde, were significantly increased from 16 % to 56 % compared to normal controls, where as an increase of 17% to 47% lipid peroxidation products were observed in kidney. Tocomin administration to stressed hamsters for 10 days before and 12 h after LPS, or 24 h after turpentine or zymosan administration significantly ameliorated the hepatic and renal lipid peroxidation products, indicating a potent antioxidant property of tocotrienols.

Conclusion: In conclusion, potent antioxidant action of Tocomin (dietary tocotrienols), may be useful in preventing the infection and inflammation-induced oxidative stress as well as atherosclerosis.

Thyroid dysfunction and its relation to lipid parameters: A risk factor for Coronary artery disease in Indian population.

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BACKGROUND : The association between overt hypothyroidism (OH) and altered lipid profile is well known, however the significance of dyslipidemia in subclinical hypothyroidism (SCH) remain controversial. The aim of this study was to evaluate the lipid profile of patients with different degrees of hypothyroidism.

METHODS: Serum lipid parameters of 47 patients with OH and 77 patients with SCH (serum thyrotropin [TSH] concentration>5.6 mU/L) were compared with 120 age- and sex-matched euthyroid controls in a cross-sectional study. We also tested whether serum TSH, Free T4(FT4) and free T3(FT3) concentrations were correlated with total cholesterol(TC), low-density lipoprotein cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL-C), high-density lipoprotein cholesterol (HDL-C), LDL-C/ HDL-C, TC/ HDL-C
RESULTS: There was a significant statistical difference (p<0.05) between the OH patient and control groups for TSH (42.301± 30.499 vs. 2.428 ± 1.210), FT4 (0.4282 ± 0.1532 vs. 0.943 ± 0.2895), FT3 (2.604 ± 0.499 vs. 3.205 ± 0.456), TC (260.043 ± 75.105 vs. 184.194 ± 45.768), TG (171.761± 137.97 vs. 118.452 ± 68.653), LDL-C (163.929 ± 44.904 vs. 111.637 ± 53.419), HDL-C (38.50 ± 8.214 vs. 52.765 ±15.591), LDL-C/ HDL-C (4.409 ± 1.449 vs.2.636± 2.215) respectively. A significant statistical difference was also found between SCH patients and euthyroid controls for TSH (13.394 ± 15.771,p<0.001), TC (236.724 ± 82.57,p<0.01), VLDL-C (33.00 ± 16.993,p<0.01), and TG (165 ±84.965,p<0.01). No statistically significant difference was found between these two groups for HDL-C, LDL-C, LDL-C/HDL-C, and TC/HDL-C. The mean levels of atherogenic lipid variables were greater in OH than in SCH, although the differences between OH and SCH did not reach statistical significance. Serum TSH, FT4 and FT3 were not significantly correlated with any of the lipid parameters across all participants.

Conclusion: We concluded that hypothyroidism is associated with changes in lipid profile. Moreover, SCH leads to an intermediary lipid profile between euthyroid individuals and that found in overt hypothyroidism. This associated hyperlipidemia may explain the observed increased risk of coronary artery disease in overt and subclinical hypothyroid patients.

Immune Detection of oxidized HDL

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Cardio vascular benefits of high HDL are well documented. Although Indians have normal or high HDL, they also have a predisposition to CVD. The evidently high risk seen among Indians is attributed to many factors like ethnicity, diet, urbanization and sedentary life style. The only indicators to define risk at the lab levels are the lipid profile numbers. It was generally believed that high LDL-C was bad and high HDL-C was good. However this simplistic view has drastically changed.

Our previous studies have shown that HDL can also undergo modification like oxidation and non enzymatic glycation. Modified HDL was shown to have lost its Paraoxonase activity without affecting the quantitative amount of HDL-associated cholesterol.

In this study we have purified HDL by heavy metal salt precipitation and affinity chromatography. The HDL was subjected to Cu ++ catalysed oxidation. It was used to raise antibodies in the egg laying hens. The IgY was partially purified and used.

IgY was shown to give a precipitin band with oxidized serum and even normal serum in ouchterlony double diffusion assay. When it was mixed with serum it precipitated protein presumably oxidized HDL.
While the precipitated HDL had about 5% cholesterol, it did not have any Paraoxonase activity when tested with paraoxon as substrate. After precipitation, the PON activity of the supernatant increased by 5 to 15%. However qualitative differences could not be identified by electrophoresis between HDL in the supernatant and HDL in the precipitate. When pooled precipitate was tested for PON activity it had detectable level of PON activity.

Our results suggest that the antibody to oxidized HDL cross reacted with the normal HDL to a small extent. However, removal of the oxidized HDL from the normal HDL improved the PON activity.

A Study of Sedentary Lifestyle among college students in East Delhi

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Introduction: Lifestyle diseases like CHD, hypertension, and diabetes are increasing significantly in India. A multi factorial causation may be attributed to the diseases, however changes in physical activity figures prominently as an important modifiable factor.

Objective: To study the prevalence of sedentary lifestyle amongst college students in East Delhi and its epidemiological correlates.

Study Design: Cross-sectional study.

Setting: A medical, nursing and general college (total three colleges) in East Delhi. Participants: 150 college students, aged 17-24 years.


Results: The students comprised of 98 (65.3%) females and 52 (34.7%) males. The female preponderance was due to nursing students being only females. Using standardized equations for calculating physical activity across the domains of work, transport and recreation, 85 (56.7%) students were found to have high physical activity, 28.0% had moderate while 15.3% had low activity level. Low levels of physical activity were found to be significantly associated with higher age group (p=0.01), being a hosteller (p=0.025), being in higher year of college (p=0.003 for trend). Proportions of low physical activity were more among MBBS (22.0%) and nursing students (18.0%) than the Arts students (6.0%), and among males (23.1%) as compared to females (11.2%).

Conclusion: A significant proportion of the students were found to have low physical activity. There is a need to offer health promotion for the prevention of future catastrophic burden of CHD and other lifestyle disorders among the young generation.

Keywords: physical activity, sedentary lifestyle, college students
Anti-atherosclerosis potential of an Ayurvedic herb; *Sida rhomboidea*.roxb: *In vitro* and *in vivo* evaluations in experimental models.

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**Introduction**: *Sida rhomboidea*. Roxb is an ayurvedic herb pandemic to the Indian subcontinent and is used as a therapeutic agent against variety of ailments including cardiovascular diseases. Previous studies from our laboratory have documented its lipid lowering, anti-obesity, anti-diabetic and cardioprotective properties. The data envisaged herein highlights its anti-atherosclerosis potential using *in vitro* and *in vivo* experimental models.

**Methods**: In the present study we evaluated possible protective role of SR against *in vitro* cell free and cell mediated LDL oxidation, foam cell formation, monocyte to macrophage differentiation and Ox-LDL induced oxidative stress and apoptosis in macrophages. Also, *in vivo* study was conducted to evaluate role of SR in prevention of *in vivo* LDL oxidation and atheromatous plaque formation in thoracic aorta.

**Results**: SR was successfully able to mitigate the key steps in induction of *in vitro* and *in vivo* experimental atherosclerosis primarily by reducing the oxidative damage and thus preventing the sojourn of physiological events.

**Conclusions**: Present study is the first report on anti-atherosclerosis potential of SR and also justifies its use as a medicine to treat cardiovascular diseases.

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Prevalence of methylenetetrahydrofolate reductase (mthfr) single nucleotide polymorphisms in patients of acute ischemic stroke

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**Introduction**: Hyperhomocysteinemia is considered as a risk factor for various cardiovascular disorders including stroke. We investigated acute ischemic stroke patients for the presence of three single nucleotide polymorphisms (C677T, A1298C and T1317C) in methylene tetrahydrofolate (MTHFR) gene as possible contributing factors for hyperhomocysteinemia.

**Method**: The presence of C677T, A1298C and T1317C methylene tetrahydrofolate reductase (MTHFR) gene single nucleotide polymorphisms (SNPs) was evaluated in 60 diagnosed cases of acute ischemic
stroke and 60 age and sex matched healthy controls. The MTHFR genotyping was performed using the polymerase chain reaction followed by restriction enzyme analysis. Serum homocysteine levels were determined in all subjects by ELISA technique.

Results: Homozygosity for the MTHFR A1298C SNP was detected in 6.66% (4/60) cases and 5% (3/60) controls respectively, whereas 6.66% cases as well as controls were heterozygous for this SNP. Homozygosity for the C677T MTHFR SNP was detected in 1.66% (1/60) controls and none of the cases. The frequency of the C677T heterozygotes was 18.33% (11/60) in both cases and controls. None of the cases and controls was homozygous for T1317C MTHFR SNP but 5% of cases were heterozygotes. Serum homocysteine was significantly raised in stroke patients but no correlation was observed with any of these SNPs.

Conclusion: Hyperhomocysteinemia observed in stroke patients is not associated with A1298C, C677T and T1317C SNPs in MTHFR gene.

Antithrombotic and antiatherosclerotic potential of herbal compound – An experimental study

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Introduction. Researchers all over the world are exploring herbal supplements to control diabetes and its complications. In our study, we have assessed anti atherosclerotic effect of FIIc isolated from fruit pulp of Eugenia jambolana in rats orally administered with atherosclerotic (Ath) diet (1.5 ml olive oil containing 8 mg (3,20,000IU) vitamin D₂ and 40 mg cholesterol) for 5 consecutive days.

Methods. Crude aqueous extract was subjected to purification via ion exchange column chromatography that yielded FII, further purification via HPLC resulted FIIc (active principle). Rats were divided into four groups (n = 5) i.e. healthy control, Ath diet control, Ath diet + FIIc (15 mg/kg) and Ath diet + glibenclamide (600 µg/mg). After 30 days of treatment, fasting blood samples were taken to estimate blood glucose, lipid profile (total cholesterol, triglyceride, HDL-Cholesterol, LDL- cholesterol and VLDL-Cholesterol), Apolipoprotein A, Apolipoprotein B and endothelial dysfunction parameters (VCAM, Fibrinogen, total NO levels and oxidized LDL).

Results. Oral administration of FIIc to experimental rats showed significant (p<0.001) improvement in blood glucose, lipid profile, Apo A, Apo B along with Atherogenic index when compared with Ath control group. Levels of endothelial dysfunction parameters were found to near normal following treatment with FIIc. Histomorphological studies of heart and aorta also confirm the same findings.
**Conclusions.** Our study showed that FIIc treatment has a significant impact on the consequences of hyperglycemia and early stages of experimentally induced atherosclerosis. So, it can be concluded that FIIc possesses significant anti atherosclerosis activity.

**Effect of ubiquinone on myalgia associated with atorvastatin**

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**INTRODUCTION**- Statins are the most effective medications for reducing LDL cholesterol concentrations. They have been proven to decrease the incidence of adverse cardiovascular events in diverse patient populations. The primary adverse effect limiting their use is myopathy, ranging from benign myalgias to rare cases of fatal rhabdomyolysis. Statin drugs interfere with the body's synthesis of CoQ10(ubiquinone). Statin inhibits conversion of HMG-CoA to mevalonate and lowers plasma CoQ10(ubiquinone) concentrations. Myopathy may be related in part to statin inhibition of the endogenous synthesis of coenzyme Q10 (ubiquinone), an essential cofactor for mitochondrial energy production.

**METHODS**- In the present study 40 patients with Atorvastatin-associated myalgia have been given Ubiquinone 180mg daily additionally for a duration of 8 weeks. The study was conducted in the Department of Pharmacology in collaboration with Department of Medicine, S.N Medical college & hospitals, Agra.

Muscle pain severity were assessed before and after treatment, by using 0-10 numeric pain intensity scale.

**RESULTS**- Value of pain on numeric pain intensity scale, before starting treatment was 4.45± 3.23 and after 8 weeks of treatment was 3.10± 3.032

**CONCLUSION**- The results suggest that Ubiquinone supplementation significantly decrease muscle pain associated with statin treatment. Further study is needed to determine whether Ubiquinone is useful for treatment of statin myalgia.

**Leptin mediated modulation of Low Density Lipoprotein receptor(s).**

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**Introduction:** Leptin, a 16-kDa protein hormone, is a product of obese gene. It is produced primarily by white adipose tissue and also by tissues like gut, placenta, liver, and kidney. In normal individual leptin
concentration is inversely related to the body fat. Defects in leptin production or function are associated with obesity in animals and humans. Leptin resistance in human is reported as one of the causes of Obesity. Obesity also develops Type-2 diabetes mellitus and/ or associated atherosclerosis. Besides obesity, persisting hyperleptinemia from leptin resistance are also found potentially involved in stimulating other atherogenic effectors; such as induction of endothelial dysfunction, stimulation of inflammatory reaction, oxidative stress, decrease in paraoxonase activity, platelet aggregation, migration, hypertrophy and proliferation of vascular smooth muscle cells.

**Methods:** Cell culture, SDS-PAGE, Western blotting, LDL uptake, Confocal Microscopy and Inhibition of receptor expression were the part of the study.

**Result:** Expression of LDL receptor by Leptin is mediated through JAK-STAT pathway and is not regulated by SREBP2 mediated feedback mechanism. Association between LDL receptor and Insulin receptor is enhanced by Leptin concentration. Leptin is unable to influence the clearance of extra-cellular LDL particles. It has no effect on LOX-1.

**Conclusion:** More Leptin maintains LDL receptor in highly expressed state but, keeps it functionally inactive; this may be a reason of developing atherosclerosis by poor clearance of extra-cellular LDL particles.

**Role of PAPP-A and hs-CRP in early assessment of risk in females with CAD**

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**Introduction:** In women with coronary artery disease (CAD), clinical presentation is different enough from men which lead to missed or delayed diagnosis of CAD. To assess the risk of CAD, we therefore assessed pro-inflammatory biomarkers, high sensitive-C reactive protein (hs-CRP), Interleukin-6(IL-6), Intercellular adhesion molecule (ICAM-1) and pregnancy associated plasma protein A (PAPP-A) in female subjects with CAD.

**Methods:** In a case control study, we analyzed blood samples of 30 Controls, 30 cases of unstable angina (UA) and 30 cases of Myocardial infarction (MI) patients for lipid profile, Pro-inflammatory markers(hs-CRP, IL-6, ICAM-1) and Pregnancy associated plasma protein-A(PAPP-A).

**Results:** hs-CRP, IL-6, ICAM-1 and PAPP-A were highly significant (p<0.001) in MI and UA as compared to controls. On discriminant analysis of all the parameters, UA has highest coefficient factor for hs-CRP when compared to control. MI has highest coefficient factor for PAPP-A when compared to controls and UA.

**Conclusions:** Based on discriminate analysis, hs-CRP is a potential marker to discriminate cases of UA from controls while PAPP-A is the reliable marker which can discriminate the cases of MI from UA and controls.
Antihyperglycemic and Hypolipidemic effects of combined treatment with ursolic acid and rosiglitazone in high-fat diet-induced insulin resistance mice

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Introduction: High fat diet intake is accused with the emerge of modern epidemic obesity and diabesity. Ursolic acid, a natural pentacyclic triterpenoid carboxyl acid, acts as hypolipidaemics. Thiazolidinediones like rosiglitazone are improving wholebody insulin sensitivity. We hypothesized that a combined treatment with ursolic acid concentrate and rosiglitazone would correct impairments of lipid and glucose homeostasis in high fat diet (HFD) induced insulin resistance in mice.

Methods: To achieve this, we divided 72 Male C57BL/6J into six groups: Group 1: Mice received standard pellet diet. Group 2: Mice received ursolic acid and rosiglitazone. Group 3: Mice received HFD. Group 4: Mice received HFD for first 10 weeks then administration of ursolic acid with HFD for next 5 weeks. Group 5: Mice received HFD for first 10 weeks then administration of rosiglitazone with HFD for next 5 weeks. Group 6: Mice received HFD for first 10 weeks then administration of ursolic acid and rosiglitazone with HFD for next 5 weeks.

Results: The HFD diet induction leads to increased body weight gain and abdominal fat content, elevated fasting plasma glucose and insulin, as well as serum triglycerides, total cholesterol, and low-density lipoprotein cholesterol, with a decrease in high-density lipoprotein cholesterol. Hepatic TG and TC levels, as well as serum activities of aspartate transaminase and alanine transaminase were increased, suggesting a diet-induced type 2 diabetes. Combined treatment with ursolic acid and rosiglitazone improves the above changes pronounced more responses then ursolic acid or rosiglitazone alone treatment.

Conclusion: In conclusion, intake of ursolic acid/rosiglitazone may be a possible therapeutic strategy for prevention of high-fat diet-induced insulin resistance.

d-limonene ameliorates hepatic biochemical and histological alterations in nonalcoholic fatty liver disease associated with metabolic syndrome

Jesudoss Victor Antony Santiago and Namasivayam Nalini
Introduction: Nonalcoholic fatty liver disease (NAFLD) is one of the most common etiologies of chronic liver disease worldwide. NAFLD is rapidly becoming a worldwide public health problem. NAFLD is an increasingly recognized condition that may progress to end-stage liver disease. The pathogenesis of metabolic syndrome associated with NAFLD is still under debate.

Methods: This study has investigated the characteristic changes in liver pathology, hepatic lipid composition, hepatic xenobiotic metabolizing enzymes, plasma insulin, glucose, circulatory lipid peroxidation, non-enzymic antioxidant levels and β-cell mass in the pancreas in metabolic syndrome associated with NAFLD. Young male Wistar rats were fed a high fat diet (HFD; 42.2% beef tallow) together with Nω-nitro-L-arginine methyl ester (L-NAME; 80mg/L drinking water) for 8 weeks and 2% d-limonene for the final 4 weeks was used as a therapeutic intervention.

Results: HFD fed rats treated with L-NAME showed statistically (p<0.05) significant increased systolic blood pressure; heart rate; hepatic tissue lipid; lipid peroxidation byproducts concentrations; hepatic marker enzymes and hepatic phase I enzyme activities with decreased circulatory non-enzymic antioxidant concentration and hepatic phase II enzyme activities. Dietary supplementation with d-limonene reversed the HFD and L-NAME induced changes and restored all the biochemical parameters as well as liver histology.

Conclusions: These experimental evidences give new insights into the therapeutic approach of d-limonene against the development of metabolic syndrome associated NAFLD.

Perspective Nanotechnology in the Artherosclerosis Drug Designing and Development

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For much of the last century, the development in atherosclerosis was regarded as an inevitable degenerative process. With the poor variety of elastic and muscular fibers in the blood vessels. Here is a review on some common choices and nanotechnological approach related to atherosclerosis drug designing and development for treatment:

Cholesterol medications: aggressively lowering low-density lipoprotein (LDL) cholesterol, the cholesterol, can slow, stop or even reverse the buildup of fatty deposition in the arteries.
Anti-platelet medications: aspirin, to reduce the likelihood that platelets will clump in narrowed arteries, form a blood clot and cause further blockage to reduce this problem stents also used in it.

Beta blocker medications: these medications are commonly used for coronary artery disease. They lower heart rate and blood pressure, reducing the demand on heart and often relieve symptoms of chest pain. To solve this problem nanobiotechnology help in by the use of different nano metals.

Angiotensin: (converting enzyme (ace) inhibitors) these medications can help slow the progression of atherosclerosis by lowering blood pressure and producing other beneficial effects on the heart arteries.

Pro-drug design through the use of potential nanoparticles for targeted drug delivery is much sought for because of highly reduced requirements of nanoparticles and their specificity along with ability to reach finest vesels and release the drug at specific area.

**Nanotechnology: a new frontier in atherosclerosis diagnosis and treatment**

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Nanotechnology is posing itself as a frontier in disease diagnosis and treatment of atherosclerosis. Challenging research in this field over the past decade has resulted in the pre-clinical trial and molecular device that targets the cellular component of atherosclerosis. Deliberations on the development so far in the concerned areas are much need and to be reviewed and adopted keeping in mind biosafety, ethical and regulatory issues. Diagnostic uses of nanotechnology in medicine and drug design and development is another way to design tracking devices to cure the defected area.

Emergence of and advances in biosensor technology and relevant nano-analytical tools (limited to the nanoscale size range), collectively referred to as 'nanotechnology', are being applied to the diagnose and treat atherosclerosis and many other major problems in cardiovascular medicine. Nanotechnology has been used in imaging diagnostic devices in cardiology, with the use of nano-particles as contrast agents, for targeted biomedical imaging of defected areas, for detection of specific pathologic targets signalling the onset of atherosclerosis, and for tracking inflammatory events. Potential therapeutic applications include the use of nano-materials in cardiovascular devices, for delivery of drugs and bioactive molecules, or in novel technologies for reducing cholesterol accumulation and for dissolving clots by the use of stents as nano devices. The aim of this technology is to design diagnostics, drug delivery along with treatment.
By the use of nanotechnology some nano-crystals modified high density lipoproteins used to find the image of atherosclerosis. These are used as markers that bind at targeted site and show the image. Tools and devices that are used in atherosclerosis diagnosis and treatment are stents nano-wires as biosensor carbon nano-tubes.

**Role of family milieu in tobacco addiction: a pilot observation**

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**Introduction:** It is strategically important to know that whether one learns tobacco habit outside or at home from tobacco control point of view. Our hypothesis is that the seeds and lessons of tobacco habit are primarily learnt at home. Kids seeing their parents, elders and siblings, smoking, or chewing tobacco during their formative phase, become inquisitive and their mind primed, to initiate smoking, at quite young age. Once tobacco habit is acquired at young age it is difficult to get rid of it because of its addictive nature, even if someone gets a disease due to its ill effects.

**Aim:** To study the pattern of tobacco use in families of smokers and non-smokers and their potential influence on the tobacco habit in subjects and their children.

**Methodology:** A retrospective case record analysis was done in 50 subjects who had a history of tobacco usage (Group I). The prevalence of use of tobacco among the parents, siblings, and children were noted by making pedigree profile of each patient. 50 age- and gender-matched controls that did not use tobacco in any form (Group II) were also evaluated for comparison.

**Results:** Tobacco users had significantly higher rates of tobacco usage among the fathers (84%), and mothers (28%) compared to 2% and 0% in controls, respectively. There was a significantly greater use of tobacco in multiple forms in the siblings (70%) of such patients among Group I as compared to 0% in Group II controls. Prevalence rates of usage of tobacco were higher among the children (24%) of patients using tobacco in Group I as compared to the 0% in control cohort Group II.

**Conclusions:** There is a significantly greater prevalence of parents, siblings being tobacco user in patients who are tobacco users, as compared to tobacco non-users. There is also greater prevalence of use of tobacco among the children of the tobacco user compared to non-users. This has great public health implications in tobacco control program warranting intensive health education focused to entire family where elders are tobacco users. One not only inherits the habit of smoking from his parents/elders but also passes on the baton to next generation.
Optical and multimodality molecular imaging and theranostic agents in atherosclerosis

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Imaging approaches that visualize molecular targets rather than anatomic structures aim to illuminate vital molecular and cellular aspects of atherosclerosis biology in vivo. Several such molecular imaging strategies stand ready for rapid clinical application. Through this poster we will describe the growing role of in vivo optical molecular imaging in atherosclerosis and highlights its ability to visualize atheroma inflammation, calcification, and angiogenesis. In addition, we discuss advances in multimodality probes, both in the context of multimodal imaging as well as multifunctional, or "theranostic," nanoparticles. This will also provide highlights on particular molecular imaging strategies that possess strong potential for clinical translation.

Key Words: atherosclerosis • molecular imaging • optical • fluorescence • multimodality • nanoparticle

Assessment of Cardiovascular Risk Profile in Patients of psoriasis

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Background - Psoriasis is a chronic inflammatory disease associated with significant cardiovascular risk profile. However, there is paucity of data from Indian subcontinent.

Aims & objectives: To evaluate the cardiovascular risk profile in patients of psoriasis by assessing lipid profile, highly sensitive C-reactive protein (hs-CRP) and Carotid artery intima-media thickness (CIMT) and to co-relate these parameters with the disease severity/ PASI and duration.

Methods: This is a case control study involving 50 clinically and histologically diagnosed cases of psoriasis and an equal number of age and sex matched controls recruited from December 2008 to March 2010.

Results- Prevalence of dyslipidemia (total serum cholesterol (p < 0.001), LDL- cholesterol (p < 0.001), HDL (p < 0.001) and VLDL cholesterol (p < 0.001), serum triglycerides (p = 0.025)), raised hsCRP (p=0.002) and CIMT (p=0.008) were significantly higher in patients of psoriasis as compared to controls and so were anthropometric parameters like waist-circumference (p= <0.001) waist-hip ratio (p= <0.001) which are markers of obesity and metabolic syndrome.

Conclusions- Psoriasis appears to be an independent risk factor for the developmental of pre-mature atherosclerosis. Therefore all psoriasis patients irrespective of age, disease severity and duration should be evaluated to enable timely interventions targeting psoriasis as well as atherosclerosis.
Role of stress and coping in acute coronary syndrome

Rachna Devi, TB Singh, S Dwivedi, Rajat Jhamb

Aims: - The Aim of the study was to assess the role of stress and coping in the patients with acute coronary syndrome.

Materials and Methods: - The sample consisted of 80 patients (index=40 and controls=40) selected with purposive sampling method who were admitted to the CCU and surgery OPD department of Guru Teg Bahadur Hospital, Delhi, India. The tools of the study included interview schedules for sociodemographic details, assessment of biological and lifestyle related risk factors and way of coping. Presumptive stressful life events scale was used for assessment of stressful life events in the year preceding ACS.

Result: - The results of the study indicated higher average number of stressful events in the study group (mean 3.08; S.D= 1.63) compared to the control group (mean 2.08; S.D= 1.45). No differences were found in the two groups regarding their ways of coping. On biological and lifestyle related risk factors assessment deranged lipid profile was found in high frequency followed by smoking, central obesity, hypertension, diabetes mellitus and family history of illness in the CAD group. The significant correlation was found between stressful life events score and the smoking among the various biological and lifestyle related risk factors.

Conclusion: - CAD has a multifactorial origin. The traditional risk factors like smoking, dyslipidemia, obesity etc which have all been assessed in the present study play an important role in the development of CAD. Life style stress is one of the risk factors for CAD which was also strongly and independently associated with the occurrence of acute coronary syndrome. Though, it is unlikely that any single factor can lead to the development of ACS, in the patients with predisposing biological and lifestyle related risk factors, the stressful life events can increase the chances of occurrence of such an episode.
Workshop
**Workshop on Assessment of Subclinical Atherosclerosis: Issues beyond Framingham**

Dwivedi S, Bhatt S, Rajpal S, Aggarwal A, Dehgani A

Coronary artery disease (CAD) is the leading cause of mortality and morbidity in both the developed and developing world, and in particular, people originating from the Indian subcontinent. Urban lifestyle particularly smoking / tobacco, stress, physical inactivity, faulty diet, family history of vascular disease and central obesity, are the major causes of its rapid spread. Males are dominantly affected; however females are no longer immune. Alarmingly, CAD occurs much earlier in Indian people. As atherosclerotic process starts in early childhood, effective preventive measures are to be started quite early. This requires assessment of cardiovascular risk selecting high risk patients harbouring subclinical atherosclerosis.

Currently prevalent risk scoring systems like Framingham Risk Score, ESC Score, Prospective Cardiovascular Munster (PROCAM) Score have several limitations especially when applied to Indian subjects. First, existing tools predict the degree of risk less well in certain ethnic groups (e.g. South East Asians), men and women younger than age 30 or older than age 65, and diabetic persons. Secondly, they do not include the established and potential risk factors like smokeless tobacco and gutkha and socio-economic status which have great relevance to Indian people, blood glucose level, triglycerides, body mass index, waist circumference, and family history of premature cardiovascular disease. Further, they do not predict risk beyond 12 years and have not incorporated lifetime risk into tools for clinical risk estimation. Moreover, they fail to identify high risk patients by actual documentation of sub clinical atherosclerosis using non invasive tools like measurement of carotid intima media thickness (CIMT) provides real time evidence of sub clinical atherosclerosis.

Our hypothesis is that simple work up regarding smoking/ tobacco, family history of premature cardiovascular disease employing pedigree details, stress, waist size, blood pressure, blood sugar, cholesterol, ECG and CIMT in high risk cases is a cost effective method to predict future risk and recurrence. Such high risk subjects need to be picked up in adolescence itself and educated regarding their life style, diet and physical activity to mitigate their propensity for future acute coronary episode.

Keeping this in view, we have organized this workshop to elucidate how simple tools like pedigree profile detailing smoking habits, alcohol, hypertension, diabetes family history of vascular disease and CIMT helps in coronary risk assessment of asymptomatic subjects. Here are few illustrative examples to be discussed in this workshop.

**Case1**

**An elderly with syncope**

RRP, a- 62- year- old, gentleman, otherwise asymptomatic, developed sudden blackout and syncope during an episode of acute infective diarrhea. Immediate ECG and electrolyte did not reveal and sign of
ischemia and of electrolyte imbalance. He was a non smoker, non alcoholic and normotensive (BP 130/80 mm/Hg) euglycemic individual. However his blood sugars (FBS, PPBS) were in pre diabetic range. Glycosylated Hb (HbA1C) was 6.7. Lipid profile showed raised cholesterol (214 mg/al), LDL-C 145mg/al, TG (168mg/al) and a borderline HDL (40mg/al). Thyroid function studies were suggestive of hypothyroidism: TSH – 122.61 mlU/L (n=0.49-4.67 mlU/L) T3<-1.25p mol/L (n=0.49-4.67), T4<5.2pmol/L (n=9.1-23.8).

Suspecting it to be a case of asymptomatic hypothyroidism associated with dyslipidemia and sub-clinical coronary artery disease, an Echo was performed. It showed normal systolic function (LVEF+69%), good diastolic compliance (E/A ratio 0.85) and normal regional wall motion. Aortic valve showed evidence of sclerosis. TMT and Thallium scan revealed reversible infero-lateral ischemia. Carotid ultrasound revealed intima media thickness of 0.9mm and a soft plaque measuring 4mm in the right internal carotid artery which was haemodynamically insignificant. Brachial flow mediated dilatation was 8% only. Abdominal aorta also showed evidence of plaque. Ultrasound of the liver, kidney and pancreas was normal.

Case 2:

A, 29 yr old junior physician, with BMI of 29 and waist of 107 cm was noted to be a cigarette smoker (3/day for 8 yrs). His blood pressure was 142/96 mm/ Hg. Coming from a non tobacco family he started smoking and social drinking on persuasion and poking of seniors. He also suffered an infective disease in the past His hairs have started graying.

Case 3

A -52-year-old male with xanthoma disseminatum and his son

A -52-year-old male auto driver presenting with acute chest pain and extensive striate xanthaelasma. He had similar type acute chest pain 7 year back which was diagnosed to be CAD. He was a mild smoker before the first episode of chest pain and had left smoking since then. Diagnosed to be hypertensive 2 years back he did not take regular treatment. Physical examination revealed xanthaelasma palpebrum both eyes more marked on the lateral canthus. There were striate type of xanthomatous lesions on flexor aspect of right and left cubital fosse, on patellar surface of knee joints and on posterior triangle of neck. Denied any similar swelling in immediate family members. He had premature graying and balding, acanthosis nigricans, skin tags on the neck and manifest central obesity (Waist-93 cms.). His right hand brachial was weaker than left brachial. ECG features were consistent with acute extensive anteroseptal STEMI. Echo revealed LV HK, LVEF-25%, MR ++ and grade 2 diastolic dysfunction. CIMT - showed plaque in right CCA and left CIMT .097 mm. Serum turned turbid and opalescent suggesting dyslipidemia. He has dominantly hypercholesterolemia (Cholesterol-292 , triglycerides- 147 mg/dl) while his 30- year –old son who too is an avid gutka chewer with features of stomatitis nicotiana has raised cholesterol, triglycerides and low HDL (Cholesterol-150, triglycerides- 167 and HDL- 36 mg/dl). Interestingly wife of index case has bilateral xanthaelasma and she too consumes tobacco and gutka. Her triglycerides have been found to be raised while HDL-cholesterol is low (Triglycerides - 202, HDL-37 mg/dl). The coronary risk and CIMT profile of the son would be discussed.
Case 4

A 35-year old male with acute retrosternal discomfort, ‘ghabrahat’ associated with extensive bilateral xanthelasma and his brother

A 35-year old male, non-smoker, non-tobacco user, tea totaller, not a known case of hypertension or diabetes, embroidery worker by profession, presented with complaints of retrosternal discomfort, ‘ghabrahat’ and sweating for one hour. His father had died of CAD at 40 years of age. Clinical examination revealed evidence of extensive bilateral xanthelasma and gynoid obesity (Fig.). His blood pressure was 112/76 mmHg on presentation. The ECG was suggestive of inferior wall ST elevation MI. His fasting blood sugar was 97 mg/dl and 2 hour postprandial blood sugar was 104 mg/dl, total cholesterol 217 mg/dl, HDL-C 24 mg/dl and triglycerides 124 mg/dl. The patient’s CIMT was normal. On detailed enquiry, his mother and younger brother also had evidence of xanthelasma. The cardiovascular risk assessment of the younger brother would be discussed.

Case 5

A 65-year old female with peripheral vascular disease, diabetes and extensive vascular disease

A 65-year old female an old patient of peripheral vascular disease for 15 years and had undergone amputation of three digits in right toe presented with chest pain this time. She had left smoking 15 years back however had undergone severe stress because of the death of spouse who was alcoholic and smoker; and death of two sons. ECG showed ST depression. CIMT showed multiple plaques in both carotids. She was also found to be diabetic and hypertensive.

This case highlights the importance of cutaneous signs of PVD as markers for CAD and also stress may be important factor in causing CAD.

Case 6

A 50-year old female with acute chest pain and her two children

A 50 year-old female from poor socioeconomic status and a known diabetic and HTN for 20 years developed acute chest pain following altercation with her alcoholic son about a year back. ECG revealed acute inferior myocardial infarction (MI) and complete heart block. She was an avid oral tobacco and gutkha chewer. She received conventional anti diabetic, anti hypertensive and anti ischemic drugs; aspirin. However, due to economic reasons she could not afford pacemaker and she left anti diabetic and statin treatment after nine months of first episode of acute MI but continued chewing tobacco and gutkha.

Very recently she again developed acute chest pain, restlessness and sweating following altercation with her son. ECG showed persistent complete heart block along with evidence of recent onset ST depression. Trop T was positive. Detail work up of family history revealed that she had a daughter and a
son both were addicted to oral tobacco and gutkha. (See pedigree) Daughter (eldest child) who was 32-year-old had features of stomatitis nicotiana, hypertension and ECG suggesting old inferior MI; though she was totally a symptomatic. Thirty-year-old son was a poly tobacco user (bidi, gutkha and cigarette for 10 years) and heavy alcoholic for 10 year.

**Parental behavior influencing the progeny**

![Pedigree diagram]

- Old Inf MI, paan masala, gutkha 3yrs
- Stained cheeks, fibrotic ridges RT>Left
- Bidi/ gutka/ cigarette 10 years
- Alcohol 10 years
- Ganja Smoker - 30 year
- SLT 50
- SLT+ 50
- SLT+ 52
- SLT+ 45
- SLT+ 40
- No SLT
- 32
- 30
- 70

CAD, Complete Heart Block (altercation with alcoholic son on two occasions and each occasion followed by ACS) ACS, CAD, CHB

Left treatment last 3 months, no anti diabetic, no statin could not afford pacemaker because of financial constraints, however she continued taking tobacco.

**Case 7**

**A - 30-year old young boy with mild chest discomfort and his pedigree**

We had the opportunity to observe and assess the three generations of a family over a period of fifteen years. We collected information by verbal autopsy methods in individual and made detail
cardiovascular assessments in both parents of index case, 8 of his siblings and one child in third generation. Thus a total of 12 members were examined and assessed in detail (Fig 1).

The son of the index patient in the third generation over the period of years, passing through phase of prehypertension, had now developed hypertension besides central obesity. He recently attended the hospital for mild chest discomfort which was not anginal in nature. He had sedentary life style and dyslipidemia.

The advantage of preparing such a detail pedigree chart is to have a snap shot view of the evident and simmering risk factors in the family as a whole and not a mere study of conventional risk factors. It elucidates the hidden stressors and hereditary factors responsible for cardiovascular disease in the family. Making such a comprehensive chart provides a definite basis for initiating primary preventive measures in high risk sibling and progeny of affected patients at the earliest opportunity. Preparing a pedigree chart of this kind is obviously a cost effective way of tackling rising trend of the cardiovascular disease in developing economy.

Case 8

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YEAR 2009
44 yr
Non smoker
BP 122/84 (mm Hg)
BMI 29.5
WHR 1.02
Dyslipidemia

YEAR 2009
41 yr
Non smoker
BP 110/66 (mm Hg)
BMI 28.6
WHR 1.04
Dyslipidemia

YEAR 2009
44 yr
Non smoker
BP 122/84 (mm Hg)
BMI 29.5
WHR 1.02
Dyslipidemia

YEAR 2009
37 yr
HTN (elev Hct)
BMI 30.49
IGF 0.88
Lp (a) 4.4
Hcy 33.54
Fibromagen 286
WHR 1.01
Gray, bald, skin tag

YEAR 2009
44 yr
Non smoker
BP 122/84 (mm Hg)
BMI 29.5
WHR 1.02
Dyslipidemia

YEAR 2009
44 yr
Non smoker
BP 122/84 (mm Hg)
BMI 29.5
WHR 1.02
Dyslipidemia

YEAR 2009
44 yr
Non smoker
BP 122/84 (mm Hg)
BMI 29.5
WHR 1.02
Dyslipidemia

YEAR 2009
44 yr
Non smoker
BP 122/84 (mm Hg)
BMI 29.5
WHR 1.02
Dyslipidemia

YEAR 2009
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BMI 29.5
WHR 1.02
Dyslipidemia

YEAR 2009
44 yr
Non smoker
BP 122/84 (mm Hg)
BMI 29.5
WHR 1.02
Dyslipidemia

YEAR 2009
44 yr
Non smoker
BP 122/84 (mm Hg)
BMI 29.5
WHR 1.02
Dyslipidemia
A 50-yr-old lady presented with acute vomiting (3 episodes) and acute chest pain radiating to left arm and shoulder with ghabrahat and palpitation. She had pain in B/L lower limbs which was burning in nature. She was diagnosed to be having diabetes (T2DM). A year back she had retrosternal chest pain and had severe burning in both lower limbs suggestive of peripheral arterial disease (PAD). Due to which amputation of fourth digit of left lower limb was carried out. She was also diagnosed as a case of hypothyroidism and put on eltroxin. 5 months back she again had episode of chest pain. ECG showed inferior wall ischemia. She is non smoker, non alcoholic, however used to apply gul tobacco for teeth burning.

Her blood pressure was 130/86 and pulsations in left lower limb were barely felt (popliteal+ anterior tibial + dorsalis pedis). Amputation of left lower limb forth digit with old healed scar mark was noted. Sensations were decreased both for touch and vibration in bilateral lower limbs.

Issues related to good control of diabetes, diffuse vascular disease and her tobacco chewer adult son need to be discussed.

Case 9

A 30-year-old auto driver a poly tobacco user who had sustained anterolateral STEMI presented with recurrence of acute chest pain. He had stopped anti ischemic treatment at his own, however continued smoking bit less and gutkha chewing. His waist was 92 cm, BMI and sugar was in prediabetic range. ECG showed fresh ST-T changes carotid IMT was. Homocysteine was raised. The issues beyond what Morris et al 1953 attributed for London bus drivers getting CAD more frequently than conductors and Framingham risk scoring needs to be addressed.

Case 10

Cardiovascular risk assessment of a 20-year-old Sikh boy whose mother had hypertension and CAD was done as part of pedigree work up. He was carpenter by profession (sedentary job) and used to take alcohol and gutkha every day for last 4 years. His BP was 110/70, waist 88 cm and fasting blood sugar was 109.
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