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HCFI Round Table Environment Expert Zoom Meeting on "Challenges in Municipal Waste Management"

JANUARY 1, 2023 (SUNDAY, 12 NOON – 1 PM)

- Rapid urbanization and changes in lifestyle have converted small town to cities and cities to mega cities. This has resulted in generation of huge amounts of municipal solid waste, which has posed a threat to the environment.
- According to the Constitution of India, solid waste falls under the purview of the state government with tasks assigned to the urban local bodies.
- The collection and disposal of municipal solid waste is carried out by the municipal body. The state government and the pollution control board acts as the regulatory authorities.
- Municipal solid waste is a neglected issue in India even though the management rules were introduced in the 2000s. The biggest drawback is that we are not aware of the rules.
- In the Solid Waste Management Rules, 2016, the focus was on segregation of waste and waste to energy plants, responsibilities of bulk generators and Resident Welfare Associations (RWAs) were assigned, non-governmental organizations (NGOs) were involved.
- From 31st December, 120 micron plastic bags have also been banned.
- Unless waste is segregated, the problem is not going to be resolved. Segregation should be done at source, not after mixing of waste. Awareness is required for segregation at source.
- In recent years, technologies have been developed, which have helped to reduce the quantum of waste. Despite the rules and availability of technologies, implementation is lacking. A reason put forth for this the nonavailability of land, which is due to the NIMBY (Not In My Backyard) syndrome.
- Data of different bodies do not match. The information is incomplete. No auditing of processing plants is being done.
- Despite rules, land, finance, we are failing. It is very important to go to the root of the problem. A uniformity in systems is needed.
- Waste management is the responsibility of all, not just the government.
- People need to be given some incentive for participation in waste management and for Bhagidari schemes to be successful. However, incentives may not be a long-term solution to the problem.
- Some value has to be added to the waste for people to take interest. But some things need to be mandated so that they are complied with.
- There is a need to bring about a culture change in the society.

- Religious waste – flowers, havan samagri should be collected from temples.
- A 100 cities have been selected for smart cities. Smart cities need smart vision, smart decisions and the ability to take people into confidence.
- The contribution of informal sector towards waste management is not recognized. The scale of work done by the informal waste collectors in India is unmatched.
- Cities have privatized waste management leading to the loss of livelihood for a number of waste pickers.
- Municipal solid waste consists of the everyday items that are used and thrown away. It mainly comes from homes, schools, hospitals and public places. Categorically the wastes are considered household, office and retail wastes.
- Concern about improper management has led to global efforts to reorient municipal solid waste management systems towards sustainability given the limited resources for its funding and the need for social admissibility aligning the incentives of the main stakeholders.
- In selecting vehicles for waste collection two errors are commonly made. One of them is to choose advanced compactor trucks when they are not suited to the local conditions especially standards of maintenance, type of waste, financial capacity of the operator and access roads. The other common lapse is to use vehicles that are designed for materials that have a much higher density than solid waste. So, that the load-carrying capacity is too small and the productivity is low. Another problem with many waste collecting vehicles is that the waste must be lifted high to get it into the vehicle and no suitable mechanism is provided to do the lifting. So, it is done manually in an inefficient and unhygienic way.
- The challenge of proper municipal solid waste management is complicated by several external stressors such as economic growth, which leads to waste generation; some of the waste such as electronics may be difficult to recycle. Population growth also increases waste generation. Densely populated towns and cities make it difficult to collect waste.
- Lack of funds is a major problem. The shortage may restrict operational expenditure, such as maintenance, fuel and salaries or there may be a lack of capital for purchasing new equipment and vehicles.

Participants: Mr Vivek Kumar, Dr Anil Kumar, Dr SK Gupta, Dr Dipankar Saha, Mr Pradeep Khandelwal, Mr Neeraj Tyagi, Mr Lovekesh Chandra, Ms Ajeeta Agrawal, Ms Neena Gupta, Dr S Sharma

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The First Gene Therapy for Bladder Cancer

Patients with high-risk non-muscle-invasive bladder cancer (NMIBC) not responding to intravesical bacillus Calmette-Guérin (BCG) therapy now have a new treatment alternative to cystectomy, which has almost always been their only treatment option. The US FDA has approved the first gene therapy "nadofaragene firadenovec-vncg" for the treatment of adult patients with high-risk BCG-unresponsive NMIBC with carcinoma *in situ* with or without papillary tumors.[1,2] Nadofaragene firadenovec-vncg, available as Adstiladrin, is a nonreplicating adenoviral vector based gene therapy and is instilled into the bladder through a urinary catheter once every 3 months for 1 year. "The adenovirus vector enters the cells of the bladder wall, releasing a gene that directs the cells to secrete high quantities of interferon alfa-2b, a naturally occurring cancer-fighting protein".[2]

Contraindication: Immunosuppressed patients or those with immunodeficiency.

Side effects: Fatigue, chills, fever, bladder discharge, bladder spasm, urgency, hematuria, dysuria.

Nadofaragene firadenovec-vncg is expected to be available in 2023, in the later part of the year. The cost of the therapy is yet to be revealed.

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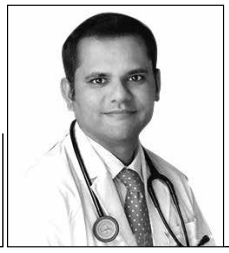

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Osteocrinology: Insights from the Great Indian Epics

ABSTRACT

Indian epics are a storehouse of knowledge and information, which offer an insight into various aspects of health and disease. In this paper, we surmise some of the legendary figures in the great Indian epics, who possibly could have disorders related to osteocrinology. Based on the detailed description provided in Vedic texts, these exemplars from Indian history provide an interesting framework for the study of osteocrinology. These may spark an interest in students and researchers to explore and understand this subject in greater depth.

Keywords: Osteocrinology, Indian epics, metabolic bone disease, Mahabharata, Ramayana

The depth and details of description provided in the great Indian epics provides an opportunity to study and reckon one of the earliest descriptions of medical disorders in history. Modern endocrinology also finds echoes of contemporary diagnosis and management in these ancient literary classics.[1,2] Numerous characters and events in the Ramayana and Mahabharata have previously been related to endocrine disorders involving the hypothalamic-pituitary axis and the reproductive system in relation to reproductive endocrinology.[3] Osteocrinology is a rapidly upcoming subspecialty of endocrinology, which deals with management of metabolic bone disease (MBD). In this paper, we surmise some of the legendary figures in the great Indian epics who have been suspected to have disorders related to osteocrinology. This is based on the detailed description provided in these Vedic texts.

The earlier descriptions of osteocrinology date back to 1000 years BC. The Egyptian God Bes and Aesop have been depicted to have achondroplasia and an Egyptian mummy dating back to 1000 BC has been described with osteogenesis imperfecta.[4] In the first century AD, the Greek physician Soranus described bone deformity in infants.[5] Daniel Whistler from England described rickets in 1645, and in 1876, Paget described osteitis deformans, later to be known as Paget's disease.

EXAMPLES FROM THE GREAT INDIAN EPICS

Indian literature, which predates these milestones, offers a picture of MBD through the portrayal of its characters. Several examples have been cited below from Ramayana, Mahabharata, Bhagavata Purana, etc.

Manthara

Manthara, Kaikeyi's housemaid in the Ramayana, is described as having a hunchback.[6] This is further supported by another less commonly cited story wherein she broke her knee while Rama was playing in the garden and struck a stick on her leg. These examples suggest that she had a probable fragility fracture and a hunchback could be indirect evidence of multiple vertebral fractures. Since she was old when she has been shown to have these features, it is likely these may have been secondary to postmenopausal osteoporosis. Moreover, they were not life-threatening as she has been mentioned to survive the entire period of exile that Rama had spent outside Ayodhya.

Kubja

A similar phenotype is ascribed to Kubja, or Trivakra (three bends), a maid servant from Mathura who is healed by Lord Krishna's touch. She has been believed to be a reincarnation of Surpanakha in Rama's time and is mentioned in other scriptures as having a hunchback. Given her younger age, reversibility and bony deformities it probably could represent a treatable cause of osteomalacia.[7]

Shakuni

Other example of a possible MBD can be considered as a differential diagnosis of Shakuni's phenotype. Shakuni, also known as Saubala, walked with a limp, purportedly due to his father striking him on the thigh, to remind him of the pain his brothers had experienced. Moreover, there is also a mention of a prolonged imprisonment with limited food for Shakuni during early days. This may have induced a nutritional osteomalacia in him predisposing to develop a permanent deformity following the traumatic injury by his father. His intelligence and strong political farsightedness is well known.

Ashtavakra

MBD is not confined to persons from lower socio-economic strata, or to characters depicted as villains. The saga Ashtavakra (eight bends) was cursed *in-utero*, and was born with eight physical deformities. A man of wisdom, he wrote the Ashtavakra Gita, which is a seminal work on dualistic philosophy. Osteogenesis imperfecta is one diagnosis which is definitely plausible. Among other causes of juvenile osteoporosis, a genetic defect, including *LRP5* mutation, may be possible.

CONCLUSION

Indian epics are a storehouse of knowledge and information, which offer insight into various aspects of health and disease. This brief compendium of osteocrinology, as described in Indian epics, creates an interesting framework for the study of the subject. Similar examples from history and mythology can be collated to spark interest in students and practitioners of medicine.

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Carboplatin Increases the Rate of Cure for Cancer

According to the report by the Tata Memorial Center, a commonly available and inexpensive drug, carboplatin, increased the cure rate and survival of a very aggressive type of breast cancer, especially among young women. In the randomized controlled trial, women with stage II to III triple-negative breast cancer were enrolled between 2010 and 2020. The enrolled women were divided into two groups.

In the study, women in the standard treatment group received standard chemotherapy consisting of once-per-week paclitaxel for 8 weeks followed by doxorubicin plus cyclophosphamide every 3 weeks for 4 cycles. In the treatment group, women received the same chemotherapy with the addition of carboplatin injections once per week for 8 weeks, given with paclitaxel. According to the study's author, the study had four major findings. Firstly, the population cure rate (5-year disease-free survival) increased by 6.6% from 64.1% in the standard arm to 70.7% in the treatment arm. Secondly, the overall survival increased by 7.6%, from 66.8% in the standard arm to 74.4% in the treatment arm. Thirdly, when the results were analyzed by age, the benefit of weekly carboplatin was almost exclusively confined to women younger than 50 years. Fourthly, the cure rate and overall survival rate increased by 12.5% and 11.2%, respectively, in women younger than 50. (*Source: https://www.daijiworld.com/news/newsDisplay?newsID=1028827*)

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REVIEW ARTICLE

Vascular Calcification in Chronic Kidney Disease

HIMANSHU VERMA*, SHAM SUNDER†, SOURABH SHARMA‡

ABSTRACT

Cardiovascular disease (CVD) is the major cause of death in chronic kidney disease (CKD). Of the various risk factors, vascular calcification has only recently come into prominence. CKD is associated with an increased risk of vascular calcification. In routine practice, clinicians usually overlook this finding. Screening for vascular calcification is often missed during first contact with nephrologists. With this article, we would like to reiterate the importance of preventing vascular calcification in early stages of CKD and once it starts appearing, its progression needs to be halted early with individualized treatment. The prevalence, sites of involvement, detection, quantification, pathogenesis, risk factors, clinical manifestations and management options have been discussed.

Keywords: Chronic kidney disease, calcification, cardiovascular disease, metabolic bone disease

The major cause of death in chronic kidney disease (CKD) is cardiovascular morbidity. Though many risk factors are thought to play a role, vascular calcification, especially coronary artery calcification is a risk factor that has only recently come into prominence.[1] CKD is associated with an increased risk of calcification which can be in form of solid organ calcification, extra-osseous soft tissue calcification or vascular calcification.[2] Vascular calcification can appear as intimal calcification, medial calcification, valvular calcification and calcific uremic arteriolopathy.

PREVALENCE

The prevalence of vascular calcification increases with advancing stages of CKD, from 40% in patients with stage 3 CKD, to 80-90% in patients with stage 5 CKD on dialysis (CKD stage 5D).[3] In 1997, Goldsmith et al had reported aortoiliac calcification in 39% patients at the onset of dialysis, with increasing risk as age advances. Also, 92% of patients had developed vascular calcification after a mean dialysis vintage of 16 years.[4]

The presence and extent of vascular calcification are notably higher in patients with CKD as compared to the general population. The prevalence was also higher in comparison to patients with other modifiable and nonmodifiable risk factors of cardiovascular disease (CVD) and normal renal function. Vascular calcification has also been described in young patients on dialysis with childhood-onset CKD, which further supports CKD as an important causative factor.

Sites of Vascular Calcification

CKD patients on dialysis have 30% to 50% risk of developing vascular calcification, the risk further increases in the elderly.[5] The blood vessels in the ankle are the earliest and most common site followed by the abdominal aorta, feet, pelvis, hands and wrist.[3] In the blood vessel, calcification can involve intima, media and occasionally both. Computed tomography (CT) has demonstrated that 80% to 100% of adult patients on maintenance dialysis develop coronary calcification.[6] Intimal calcification is part of advanced atherosclerosis and is associated with cholesterol deposition in atherosclerotic plaques. Intimal calcium deposition is principally associated with myocardial infarction and thrombotic events. It is mostly seen in the elderly. Calcium in the intimal layer may be a marker for plaque vulnerability to rupture and is associated with occlusive disease. However, there are reports that this form of calcification may actually stabilize atherosclerotic plaques and reduce risk of acute plaque rupture. In their opinion, higher load of calcium in vessel walls (intima and media) in uremic subjects may exert a stabilizing effect on arterial plaque lesions by "holding the artery open", thereby acting in many ways like an adaptive coronary stent.[7]

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Medial calcification (Monckeberg's sclerosis) may result in palpable arteries, pseudo-hypertension, isolated systolic hypertension, left ventricular hypertrophy and coronary hypoperfusion resulting in significantly adverse cardiovascular outcomes. This is the predominant type of calcification seen in diabetes and CKD.[8] Medial calcification is more common in the young, patients on long-term dialysis and those with an elevated calcium-phosphorus product (Ca × P) ratio without conventional atherosclerotic risk factors. Although it is not clear whether Ca × P is a risk factor for vascular calcification. In most cross-sectional analyses of patients with renal failure, vascular calcification has not correlated with Ca × P.[9]

Vascular calcification can lead to increased pulse pressure, reduced coronary perfusion and abnormal autonomic and endothelial vasomotor functions. Also, there is increased difficulty forming vascular anastomosis (vascular grafts or arteriovenous fistulae) or performing successful coronary artery interventions (angioplasty and coronary artery bypass grafting).[10]

Detection of Vascular Calcification

Although not clinically useful, the "gold standard" technique for the detection, assessment and quantification of vascular calcification is the histological examination of postmortem arterial specimens. Clinical detection is mostly by plain radiograph, which shows pipe stem (tram line) appearance in case of medial calcification (Fig. 1). CT scanning permits both the detection and quantification of the extent and severity of calcification. Vascular ultrasound can frequently show calcified plaques and calcified media. The use of plain lateral abdominal radiography or echocardiography to detect the presence or absence of vascular or valvular calcification, respectively has been endorsed by Kidney Disease: Improving Global Outcomes (KDIGO).[11]

Quantification of calcification is done by noninvasive radiology using electron-beam computed tomography (EBCT) and multislice spiral CT.[12] This, however, cannot distinguish between intimal and medial calcification.

PATHOGENESIS

It was formerly thought that vascular calcification is a passive process caused by elevated phosphate levels and elevated calcium-phosphorus product. It is now felt that vascular calcification is akin to osteogenesis and is an active process involving bone structural proteins and regulators of bone formation with a role for physiological inhibitors of calcification (Fig. 2).[13] There are various factors, which could put a patient with CKD at increased risk.[14]

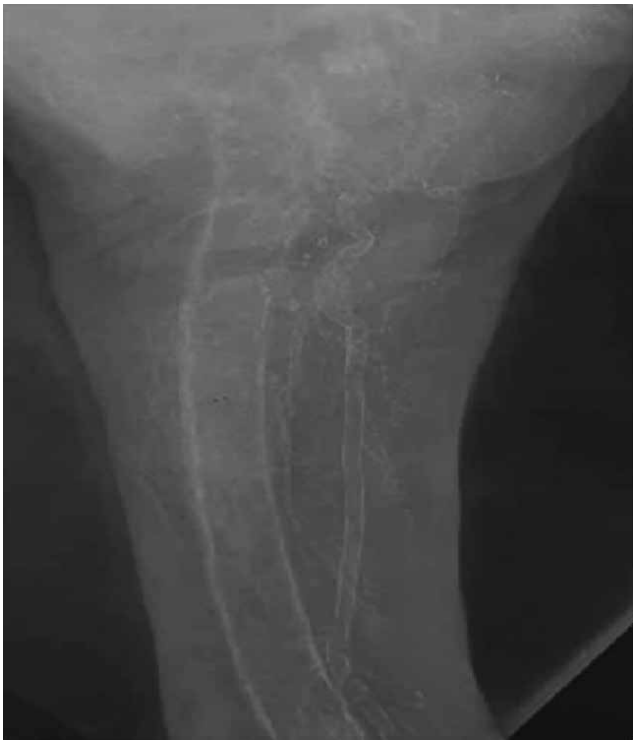

Figure 1. X-ray thigh of a patient of CKD Stage 5D on maintenance hemodialysis with CKD-metabolic bone disease showing pipe stem (tram line) appearance suggestive of medial calcification of femoral artery.

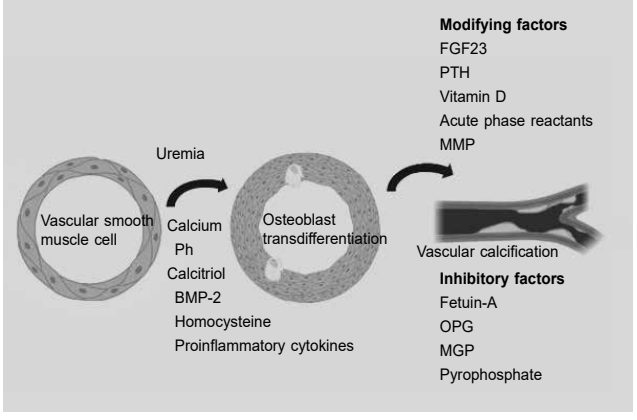

Figure 2. Molecular mechanisms favoring vascular calcification.

Molecular Mechanisms Favoring Vascular Calcification

- **Increased amounts of bone-associated proteins:** These include osteocalcin, osteopontin, matrix gamma-carboxyglutamic acid (matrix Gla) protein and osteoprotegerin. Runt-related transcription factor 2 (RUNX2) also known as core-binding factor

subunit alpha-1 (CBF-α1) are specific transcription factors for osteoblastic differentiation from their mesenchymal precursors and are now thought to play an important role in vascular calcification.[15] Elevated phosphorus levels are associated with increased RUNX2 levels.

- **Elastin degradation** in the blood vessel wall by matrix metalloproteinases favors calcification by inducing over expression of transforming growth factor beta (TGF-β).
- **Other mediators** of calcification include calcitriol, advanced glycation end products and leptin.
- **Loss of inhibitors:** Inhibitors of calcification include pyrophosphate, parathyroid hormone (PTH)-related peptide, osteopontin, osteoprotegerin, bone morphogenic protein 7 (BMP 7), matrix Gla protein, fetuin-A, etc. are lost. Low fetuin-A levels are associated with increased risk of cardiac events.[16]

RISK FACTORS

- **Dialysis vintage:** More severe calcification is associated with increased dialysis duration.
- **Age:** Risk is more with increasing age.
- **Serum phosphate:** A central role for raised plasma phosphate levels has been suggested.[17]
- **Serum calcium:** An increased intake of calcium as a phosphate binder may directly enhance coronary arterial calcification. At 1 year, among 200 hemodialysis patients randomly assigned to a noncalcium-based phosphate binder (sevelamer) or a calcium-based phosphate binder, although serum phosphorus control was similar with both agents, sevelamer was associated with a much lower percentage increase of the median absolute calcium scores in both the aorta and coronary arteries.[18] As use of sevelamer was associated with a lower calcium level, this suggests a vital role for serum calcium levels in enhancing vascular calcification.
- **Diabetes mellitus:** Diabetics are at an added risk of vascular calcification irrespective of renal status.
- **Magnesium:** Several studies have demonstrated presence of two distinct types of calcium phosphates deposits in tissues of patients with chronic kidney failure. Deposits found in periarticular calcifications are carbonate containing apatite, while those found in calcified visceral tissues are either microcrystallites of magnesium whitloekite.[19] X-ray diffraction patterns of these two types show tumoral calcification to give apatitie pattern and visceral calcification, an amorphous one. Presence of magnesium may promote formation of this latter type of calcium deposit by disturbing crystallization of apatite and stabilizing amorphous phase as observed in synthetic systems.[19]
- **Active vitamin D:** These are used in the treatment of secondary hyperparathyroidism in CKD. Low levels of serum calcitriol are associated with increased risk of calcification.[20] Calcitriol suppresses vascular smooth cell proliferation. However, clinically employed doses of vitamin D frequently result in hypercalcemia, which can accelerate extraosseous calcification. The propensity to ectopic/soft tissue calcification is also associated with adynamic bone disease due to excessive vitamin D dosing. Vitamin D therapy, when administered in excess, is a potential vascular toxin, being associated with *in vitro* phenomena that could predispose to *in vivo* plaque calcification and atherosclerosis. Thus calcitriol has a dual role in calcification. Vitamin D analogs like paricalcitol, doxercalciferol, etc. which have less propensity for increasing calcium or phosphorus levels may have advantages in preventing calcification.
- **Vitamin D deficiency:** Vitamin D deficiency appears to contribute in vascular calcification. The pathogenesis include lowered PTH-related peptide levels (which normally inhibit vascular calcification), and suppressed CBF-α1 and bone morphogenic proteins (which enhance the transformation of vascular smooth muscle cells into osteoclast). Thus, both an excess and deficiency of vitamin D can contribute to the vascular calcification via different mechanisms.[21]
- **Inflammation:** The chronic inflammatory milieu of uremia may contribute to vascular calcification. A large number of pro-inflammatory or anti-inflammatory substances have been evaluated as possible factors underlying this abnormal milieu. These include osteopontin, osteoprotegerin and fetuin. Osteopontin (a chemoattractant) concentrations in blood and in atherosclerotic plaques are increased in hemodialysis patients compared to age-matched healthy controls, and may correlate with aortic calcification score.[22]
- **Fetuin-A:** This is a calcium-binding protein found in serum and produced by the liver. Normal levels of fetuin help clear apoptotic cells, which act as potential nidus for crystal formation in medial arterial calcification by augmenting phagocytosis. Low fetuin levels, which are observed with CKD, other chronic inflammatory states and patients on

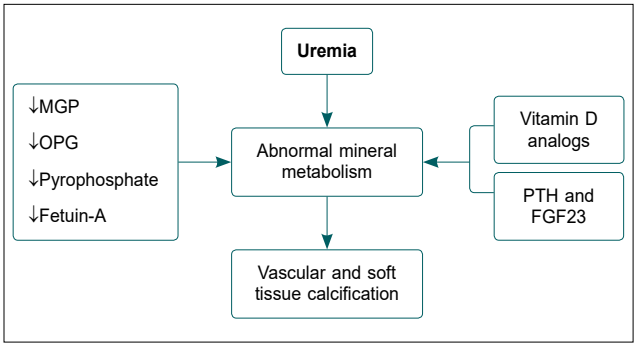

Figure 3. Pathogenesis of vascular and soft tissue calcification in CKD patients.

hemodialysis, are associated with increased vascular calcification, cardiovascular mortality and overall mortality in some studies of dialysis patients.[23]

- **Malnutrition, inflammation and atherosclerosis (MIA) syndrome:** It is now felt that the calcium phosphate deposition is not a passive phenomenon but an active one involving increased intracellular phosphate uptake, which can be enhanced in inflammatory states.
- **Premature aging-related genes (Klotho and FGF23):** Klotho is a transmembrane protein, which acts as a cofactor for fibroblast growth factor (FGF23). Its deficiency is associated with increased risk of calcification.

Other risk factors include increased C-reactive protein (CRP), hyperparathyroidism, parathyroid suppression (adynamic bone disease), decreased serum fibrinogen, hypoalbuminemia, hyperhomocysteinemia and dyslipidemia.

Figure 3 depicts pathogenesis of vascular and soft tissue calcification in CKD patients.

CLINICAL MANIFESTATIONS

The clinical manifestations may depend on the site of calcium deposition.

- An increase in systolic pressure and a decrease in diastolic pressure with an increased pulse pressure are seen mainly in those with medial calcification.
- Left ventricular hypertrophy
- Angina
- Myocardial infarction and thrombotic events. This is more common in the elderly with risk factors for atherosclerosis. Most patients have predominant intimal calcification.
- Very painful skin lesions and ulcerations following occlusion of small cutaneous arterioles. The typical picture is a mixture of large retiform ulcerations with thick eschar surrounded by violaceous, indurated, tender, retiform plaques. However, the degree of cutaneous and subcutaneous tissue involvement is highly variable and may also be rather limited to livedo reticularis or to a single indurated plaque formation. Compared to those with intimal calcification, patients with medial disease had a longer survival.

PREVENTION AND THERAPEUTIC APPROACHES

There is no evidence-based medicine treatment option available. Treatment is multimodal. The mainstay of therapy in patients with vascular calcification is the normalization of calcium, phosphorus and PTH metabolism. The following are some of the therapeutic options:

- **Sevelamer:** This drug is a cationic polymer that binds phosphate through ion exchange. lf vascular calcification is found in two or more sites, use of a noncalcium-containing phosphate binder could be considered.[24] A new variant of this drug where the hydrochloride moiety is replaced by carbonate is now available. In the "Treat to Goal Study", 200 patients undergoing maintenance hemodialysis were randomly assigned to sevelamer or calcium-based phosphate binders. At 1 year, although serum phosphate control was similar with both agents, calcium-based phosphate binders were associated with a higher incidence of hypercalcemia (16% vs. 5%) and an increased incidence of low PTH levels.[18] A reduction in levels of CRP and uric acid and oxidative stress may contribute to the beneficial effects of sevelamer. Besides, unlike calcium-based phosphate binders, sevelamer also has a bile-acid sequestrant effect, thereby reducing lipid absorption and this could have contributed to the better cardiovascular profile with sevelamer. In the RIND trial, among 129 patients with coronary artery calcium at dialysis initiation, more rapid and more severe increases in calcification were observed with calcium-containing phosphate binders at 12 and 18 months. Those on sevelamer were more likely to show stabilization or regression in coronary artery calcification at 12 months.[25] However, despite the possible decrease in vascular calcification with this agent, a well-designed prospective study DCOR, found no difference in cardiovascular mortality or total mortality among hemodialysis patients between sevelamer and a calcium-based phosphate binder.[26]

- **Other noncalcium-containing oral phosphate binders:** Lanthanum is an alternative phosphate binder, which does not increase the calcium levels and can be tried to prevent vascular calcification.
- **Vitamin D analogs:** Drugs like paricalcitol, doxercalciferol may not raise the calcium levels to the same extent as calcitriol.
- **Bisphosphonates:** Their use has been found to decrease calciphylaxis.[27]
- **Fetuin-A (endogenous inhibitor of calcification)**
- **Calcimimetics:** They seem to be promising agents for treating extraosseous calcifications. Calcimimetics successfully control secondary hyperparathyroidism in patients with CKD and concomitantly lower serum levels of both calcium and phosphate. The administration of cinacalcet permits the suppression of PTH in patients not adequately controlled with vitamin D analogs, as well as the optimal control of PTH.[28] Because of this improved biochemical control (i.e., reduced PTH without increased Ca × P), the possibility exists that the use of cinacalcet may reduce vascular calcifications and improve cardiovascular outcomes. Animal data and limited observational studies have suggested that cinacalcet may retard the progression of valvular, aortic and coronary calcification in dialysis patients.[29]
- **Renal transplantation** appeared to markedly slow down or abolish the progression of coronary artery calcification/vascular calcification in a small study.[30] However, there are also reports on progressive calcification after transplantation.[31]
- **Parathyroidectomy:** There are only occasional reports on a beneficial role of subtotal parathyroidectomy.[32]
- **Hyperbaric oxygen therapy** has been shown to improve skin lesions in patients with distal forms of vascular calcification.[33]
- **Sodium thiosulfate:** This sequesters calcium ions to form highly soluble calcium thiosulfate complexes and can prevent calcium phosphate precipitation.[34]

OUR EXPERIENCE

At our center, we screened pre-ESRD (end-stage renal disease) [CKD stage 4 and 5] patients for the presence of vascular calcification using digital X-ray lumbar spine and multislice CT scan (Fig. 4). The prevalence of vascular calcification (abdominal aortic calcification) in pre-ESRD patients was 75% (73.6% and 81.8% for CKD stages 4 and 5, respectively). The median aortic calcification index was 19.9% in all patients, 18.5% in CKD stage 4 and 21.4% in CKD stage 5. Decreased glomerular filtration rate may be associated with the presence and extension of abdominal aortic calcification in pre-dialysis CKD stages 4 and5.[35]

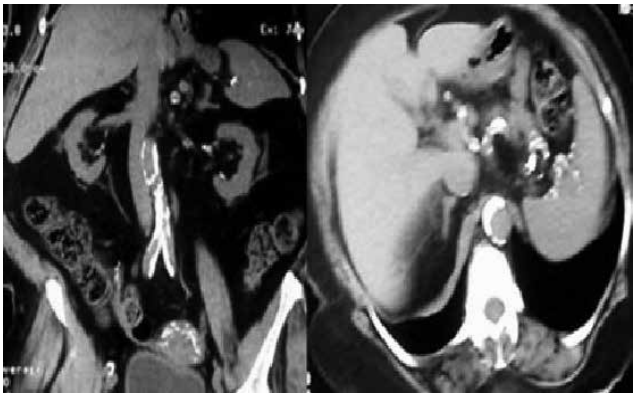

Figure 4. Multislice computed tomography image of abdominal aorta showing multiple calcification sites.

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CLINICAL STUDY

Safety and Efficacy of a Combination of Amino Acids in Insufficient Lactating Mothers

BHARTI KALRA

ABSTRACT

Milk production of the mammary gland is mainly determined by the milk synthesis and proliferation abilities of mammary epithelial cells (MECs). The availability of amino acids is critical for the production of milk. Amino acids enhance milk protein synthesis and mammary gland development through the mechanistic target of rapamycin (mTOR) pathway. Taurine enhances lactation by increasing prolactin secretion. Vitamins such as Thiamine and Pyridoxine are essential for maintaining and growing maternal and child health. However, there is a paucity of data regarding the safety and efficacy of amino acids and vitamins combination in lactating mothers with insufficient lactation. Hence, a prospective study was conducted to assess the safety and efficacy of a novel amino acids and vitamins combination. The results showed that with the intervention of this combination, 62% of participants showed onset of lactation within 45 minutes to 2 hours. The study suggests clinicians should consider this novel combination to improve lactation in insufficient lactating mothers.

Keywords: Lactation, amino acids, vitamins

Nursing infants' optimal development and health depend on their mother's milk production. During lactation, the body's normally quiescent functions become active and place a greater demand on amino acids and other substrates, which may have quantitative significance.[1] The availability of amino acids is critical in the efficiency with which milk proteins are synthesized.[2]

Increased dietary intakes and increased blood flow to the gland are responsible for a significant portion of this amino acid supply. The mammary glands massive demand for amino acids is primarily fulfilled by an increase in blood flow because the fractional rate at which amino acids are extracted increases.[3] Hence, a prospective study was conducted among lactating mothers with no or insufficient lactation to establish the efficacy and safety of a novel combination of Taurine, DL-Methionine, L-Glutamine, Glutathione, Glycine, L-Cysteine, Thiamine and Pyridoxine.

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METHODS

The study is a real-world prospective study to assess the efficacy of the novel combination and the occurrence of adverse events in lactating mothers with no or insufficient lactation. The study was a questionnaire-based study conducted among lactating mothers with no or insufficient lactation. The data was collected anonymously. Written consent was taken formally from the study participants after informing them about the study, the use of the medicine in their condition, and any related side effects that may occur. Analysis of the responses was carried out by calculation of simple percentages.

RESULTS

The study included 180 lactating mothers aged 19 to 38 years with no or insufficient milk production. Patients were intervened with two capsules twice daily for 5 days to 1 month. Most study participants reported (62%) increased milk output between 45 minutes to 2 hours (Fig. 1). With only three exceptions, most respondents gave good feedback. None of the patients reported any adverse effects after using a novel combination of Taurine, DL-Methionine, L-Glutamine, Glutathione, Glycine, L-Cysteine, Thiamine and Pyridoxine. Clinicians found it to be an effective remedy for immediately correcting lactation.

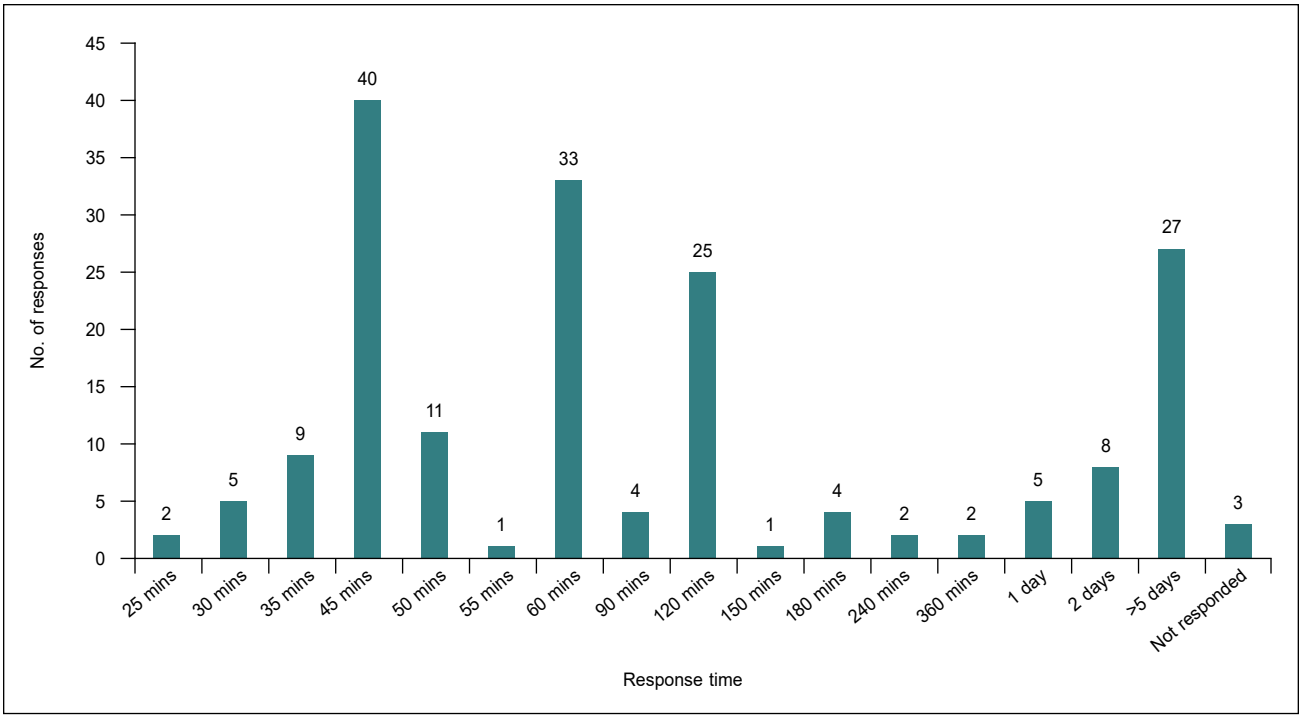

Figure 1. Post-intervention onset of lactation in the study participants.

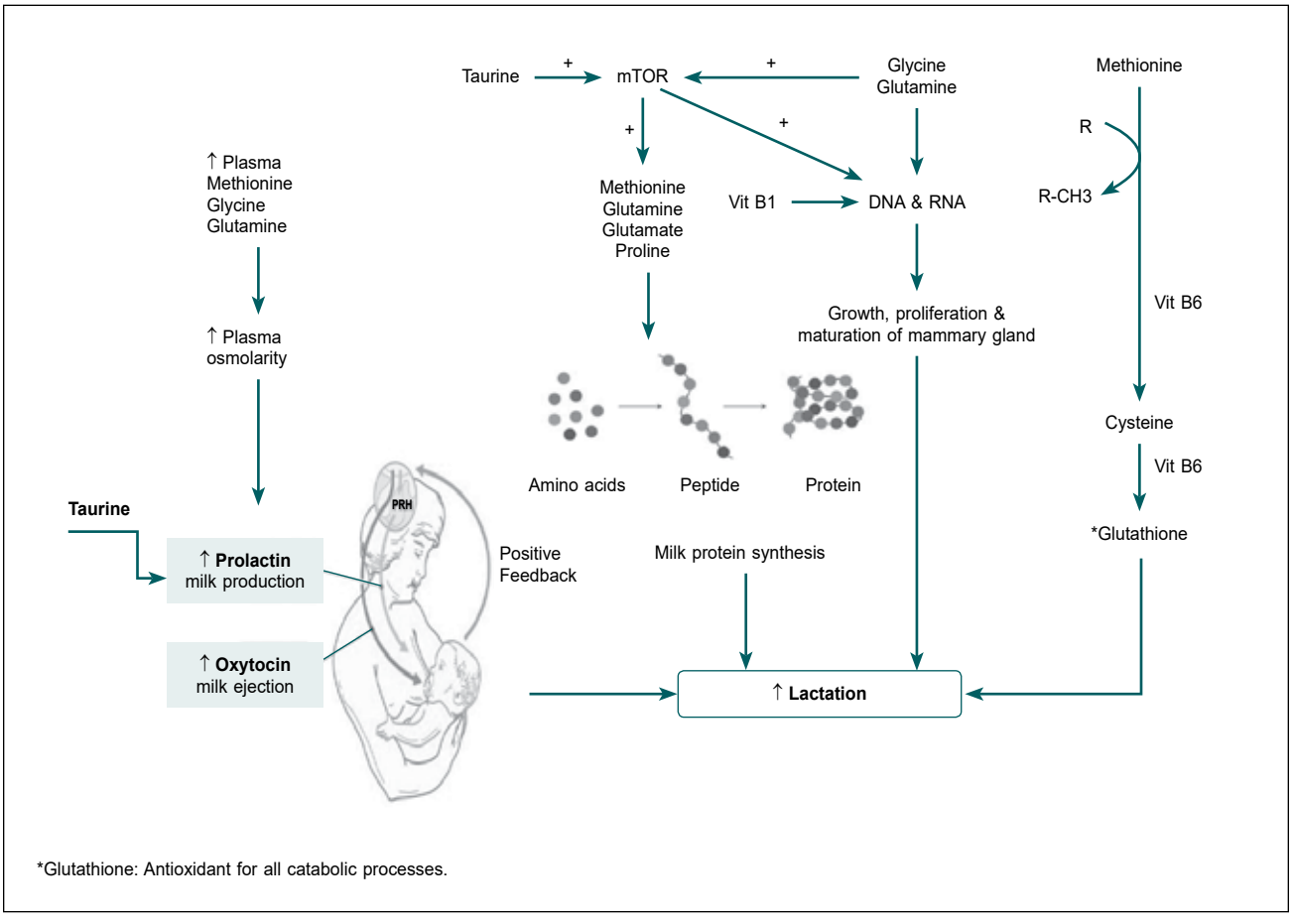

Figure 2. Role of amino acids and vitamins in lactation.

DISCUSSION

Milk production of the mammary gland is mainly determined by the milk synthesis and proliferation abilities of mammary epithelial cells (MECs). The mechanistic target of rapamycin (mTOR) is a serine/threonine protein kinase and a central hub of signaling leading to protein and lipid synthesis as well as cell proliferation. It has been reported that amino acids, growth factors, nutrients and other environmental cues regulate mTOR phosphorylation (activation).

Amino acids can directly stimulate the phosphorylation of mTOR, thereby promoting translation initiation and polypeptide formation. This results in the growth, proliferation and maturation of MECs and milk protein synthesis. Amino acids such as Methionine and Glutamine are the most important regulators of milk synthesis. Folic acid helps to maintain the Methionine pool. Methionine deficiency inhibits the mechanistic target of rapamycin complex 1 (mTORC1) signaling and reduces milk secretion.[4]

Glutamine is another milk's most prevalent amino acid for milk synthesis. Previous research indicates that lactation is accompanied by a modest catabolic state in which skeletal muscle proteins are degraded to produce more Glutamine in Glutamine deficiency.[5]

Glutathione is an essential antioxidant that eliminates free radicals produced by several catabolic processes in the brain. It prevents mood disorders, such as postpartum depression. L-Cysteine is a precursor for Glutathione.[6]

Pyridoxine is a water-soluble vitamin that treats and prevents vitamin B6 deficiency, anemia and peripheral neuropathy. Thiamine takes part in nucleic acid synthesis, helps generate energy for the body from nutrients, and aids in the growth and development of body cells. Thiamine and Pyridoxine are passed on to a nursing baby in the mother's milk.[7]

A study reported that Glycine maximizes protein accretion in milk. The findings focus on the significant implications of Glycine for newborn formulae, particularly for preterm and low-birth-weight infants.[8]

Milk production also depends on prolactin. Taurine enhances prolactin secretion. It also stimulates the phosphorylation of mTOR, promoting translation initiation and polypeptide formation.[4] Roles of Taurine, Methionine, Glutamine, Glycine, Cysteine, Glutathione and vitamins in lactation[9,10] have been depicted in Figure 2.

Orally ingested amino acids and vitamins are directly absorbed by the intestines. A set of transporters on the apical surface of enterocytes absorb amino acids from the intestinal lumen by coupling their transport with the transport of Na^+ ions. Free amino acids can be absorbed very rapidly and appear in the bloodstream within minutes, reaching peak concentrations between 30 and 40 minutes.[11] Oral supplements of vitamins and amino acids are effective, cost-effective and easy to consume and can be taken with/after food or as directed by physicians.[12,13]

Our clinical study showed that supplementation with Taurine, DL-Methionine, L-Glutamine, Glutathione, Glycine, L-Cysteine, Thiamine and Pyridoxine improves milk production in no or insufficient lactating women. A previous study by Nagarathnamma et al proved that amino acid supplementation improves lactation.[9]

Therefore, these data promote the creation of a dietary supplement, given that oral supplementation significantly increases its concentration and has beneficial effects on its total concentration in breast milk.

CONCLUSION

Our investigation suggests that the onset of action of the novel combination containing Taurine, DL-Methionine, L-Glutamine, Glutathione, Glycine, L-Cysteine, Thiamine and Pyridoxine can occur within 45 minutes to 2 hours. There are no adverse consequences. It is an oral medication; hence, it can be easily administered to the patient. This investigation confirms that the novel combination can increase milk production in inadequately nursing mothers without endangering the mother's or child's health. It is an oral medication; hence can be easily administered to the patient to improve insufficient lactation.

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CASE REPORT

Recurrent NSAIDs-induced Hypoglycemia in a Nondiabetic Patient

UTSAV SAHU

ABSTRACT

Hypoglycemia is defined by a low blood glucose level associated with clinical symptoms. Hypoglycemia may be related to treatment of diabetes, but also to drugs, alcohol, critical illness, cortisol insufficiency including hypopituitarism, insulinoma, bariatric or gastric surgery, pancreas transplantation or glucagon deficiency, or may be surreptitious. Some hypoglycemic episodes remain unexplained, and a proper drug history should be sought. Though various drugs have been implicated as a cause of hypoglycemia; herein, we report a case of recurrent nonsteroidal anti-inflammatory drugs (NSAIDs)-induced hypoglycemia in a nondiabetic patient.

Keywords: NSAIDs, hypoglycemia, diabetes

Hypoglycemia is most commonly caused by insulin or insulin-producing drugs used to treat diabetes mellitus or by exposure to other drugs, including alcohol. However, a number of other disorders, including critical organ failure, sepsis and inanition, hormone deficiencies, non-beta-cell tumors, insulinoma and prior gastric surgery, can cause hypoglycemia.[1]

Hypoglycemia may be documented by Whipple's triad: (1) symptoms consistent with hypoglycemia; (2) a low plasma glucose concentration measured with a precise method and (3) relief of symptoms, after the plasma glucose level is raised. The lower limit of the fasting plasma glucose concentration is normally ~70 mg/dL, but lower venous glucose levels occur normally, late after a meal, during pregnancy and during prolonged fasting (>24 h).

Neuroglycopenic manifestations of hypoglycemia are a direct result of central nervous system glucose deprivation. These features include behavioral changes, confusion, fatigue, seizure, loss of consciousness, cardiac arrhythmias and if hypoglycemia is severe, death.

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Neurogenic (or autonomic) manifestations of hypoglycemia result from the perception of physiologic changes caused by the central nervous system-mediated sympathoadrenal discharge that is triggered by hypoglycemia. They include adrenergic symptoms, such as palpitations, tremor and anxiety, as well as cholinergic symptoms, such as sweating, hunger and paresthesias.[2]

Severe hypoglycemia can cause serious morbidity and increase the risk for serious cardiovascular events and mortality during and after the initial hypoglycemic episode. It should be managed as a medical emergency.[3]

CASE REPORT

A 60-year-old normotensive, nondiabetic, euthyroid female developed sudden onset drowsiness, palpitations and profuse sweating at home, her blood pressure (BP) was 160/90 mmHg and random blood sugar (RBS) was found to be 47 mg/dL. She was given some sugary syrup and brought to hospital next morning where her plasma glucose by lab came out to be 54 mg/dL, serum cortisol - 40 μg/dL, serum insulin - 142.1 uIU/mL and C-peptide - 9.4 ng/mL.

Her glycated hemoglobin (HbA1c) was 5.6% and there was no positive family history of diabetes. She underwent ^{68}Ga-DOTA-NOC PET-CT to localize an insulinoma, but it was normal. The patient reported taking diclofenac 50 mg tablet for headache following which she developed low sugar. She gave history of developing low sugar levels in the last 5 to 6 years whenever she took mefenamic acid or etoricoxib tablet.

The same symptoms were reproduced again the next morning after the patient took an identical dose of diclofenac. After taking the same dose again that afternoon, she developed the same symptoms, with greater intensity and lost consciousness. Her blood glucose level was 27 mg/dL. The patient recovered fully soon after receiving intravenous glucose. She stopped taking NSAIDs and has not experienced further hypoglycemic episodes.

DISCUSSION

Hypoglycemia may occur in certain endocrine disorders, such as hypopituitarism, Addison's disease or myxedema; in disorders related to liver malfunction, such as acute alcoholism or liver failure and in instances of end-stage chronic kidney disease. When hypoglycemia is a primary manifestation developing in adults without apparent endocrine disorders, the diagnostic possibilities include hyperinsulinism, due to either pancreatic B-cell tumors, iatrogenic or surreptitious administration of insulin or sulfonylurea. A number of medications apart from the sulfonylureas can occasionally cause hypoglycemia. Common offenders include the fluoroquinolones such as gatifloxacin and levofloxacin, sulfonamides, tramadol, topiramate, pentamidine, quinine, angiotensin-converting enzyme (ACE) inhibitors, beta-adrenergic blocking agents and indomethacin.[4]

Sone and colleagues have reported a case of ibuprofen-related hypoglycemia in a patient receiving sulfonylurea.[5] Most of the previous case reports of nonsteroidal anti-inflammatory drug (NSAID)-induced hypoglycemia have been in diabetic patients already taking sulfonylureas, where it was proposed that NSAIDs may block K (ATP) channels in insulin secreting beta cells through an extracellular mechanism and thus increases insulin secretion leading to hypoglycemia.[6] But our patient was nondiabetic and developed hypoglycemia to various NSAIDs, which has never been reported before.

CONCLUSION

Hypoglycemia is uncommon in people who are not being treated for diabetes mellitus and, when present, the differential diagnosis is broad. This case report reinforces the importance of taking a thorough history and being aware of various drugs that can cause hypoglycemia to prevent unnecessary diagnostic tests.

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New Campaign to Identify TB Cases Launched in Uttar Pradesh

Uttar Pradesh: The government has launched a campaign to identify tuberculosis (TB) cases in the state with a special focus on the 15th of every month, known as "Nikshay Diwas". On the 15th, all health facilities in the state will provide screening and testing for the suspected cases. ASHA workers will run a door-to-door campaign on the day and try to identify suspected cases.

Principal Secretary of Medical and Health Affairs, Dr Partha Sarthi Sen Sharma, stated that apart from ASHA workers, Anganwadi workers, ANMs and community health officers (CHOs) can play vital roles in the campaign. Patients, once identified, will also get medicine. In the campaign, ASHA workers will bring suspected cases to the nearest health and wellness centers, and CHOs will conduct primary tests by making a provisional ID of the suspected case. According to the symptoms, the tests will include HIV and diabetes. Additionally, ASHA workers will ensure the bank details of the patients, once identified and registered, are entered into the Nikshay portal so that Rs. 500 per month of financial assistance is sent to the bank account of the patient or beneficiary. (*Source: https://health.economictimes.indiatimes.com/news/policy/up-campaign-to-identify-tb-cases/96274793*)

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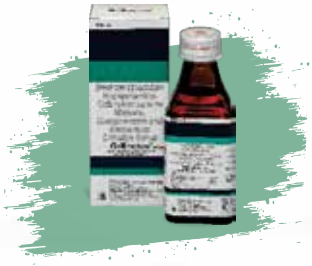

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Motivational Techniques and Hacks for Treating Childhood Obesity

MEENAKSHI VERMA*, SUNEET KUMAR VERMA†

ABSTRACT

Treating obesity in children and adolescents is not a cakewalk. Asking them directly to get up and run, or just serving them a four-quadrant plate won't serve the purpose at all. An obese child is already under the repercussions of oppressive remarks by the society. If at home as well, their mental milieu is not taken care of, there are chances of them being trapped in the shackles of depression. To avoid such drastic consequences, one must be prudent enough, while conversing with their children/patients regarding their weight. Motivation enhancement is very crucial in childhood obesity management, as the required changes in diet, behavior and physical activity are difficult to carry out with an insufficient level of motivation.[1] The motivational hacks presented here might be helpful for parents and health care professionals in convincing their children/patients to stride through the road to health.

Keywords: Childhood obesity, obesity motivation, child health, child motivation, weight control, diet, behavioral modification

Obesity in children is defined as body mass index (BMI) above certain level as per age and gender of the child. It is the result of an interplay of genetic, environmental and behavioral factors. The changing lifestyle and unhealthy dietary patterns make genetically predisposed children more vulnerable to gain weight at abnormally higher pace. The unprecedented situation during COVID lockdown has paved the way for emergence of another pandemic, especially in children, the pandemic of obesity. Childhood obesity is now a growing public health concern in India as well as other parts of the world. According to UNICEF's World Obesity Atlas for 2022, India is predicted to have more than 27 million obese children, representing 1 in 10 children globally, by 2030.[2] The social stigma of obesity puts the children at risk for discrimination, teasing, bullying and isolation along with physical afflictions like hypertension, type 2 diabetes, coronary heart disease and psychological problems including low self-esteem, poor body image and depression. Considering its adverse effects on the child's physical, psychological and social functioning, controlling this pandemic is of utmost importance.

The four pillars of obesity management are nutrition, exercise, behavioral modification and medications. However, just being well versed with the solution does not rectify the problem automatically. The real challenge is to convince the children to execute these pillars. Though medications are not recommended in children, the foundation for other three pillars is effective motivation.

APPROACH FOR MOTIVATING AN OBESE CHILD

Before discussing the hacks of motivating a child, it is extremely important to identify the correct approach for the same. Persuading a child individually to perform the actions differently while all the other family members are following their favorite routine, is never acceptable and hence the efforts go redundant.[3] A 1998 study by Golan and colleagues found that treatments that involve the parents are associated with better childhood weight control than those treatments that involve only the child.[4] Rather than isolating the child for special diets and special exercise regimens, all family members are encouraged to follow healthy lifestyle together.

LEVELS OF MOTIVATION

The grounds on which obese children must be motivated depend a lot on their level of insight into

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Table 1. Levels of Motivation of an Obese Child

Level 1 (No insight): **Motivational Interviewing** (by health care personnel)

- Be compassionate and understanding
- Replace hurtful terms with more comforting ones
- Converse empathetically
- Parental counseling
- Appointment for Level 2

Level 2 (Has insight but lacks motivation): **Motivational Induction**

- Mindful conversation by parents at home
- Family members as role models
- Physical activity hour in an activity area at home
- Sneaky ways to keep the child active
- Screen time reduction hacks
- Healthy food hacks
- Move on to the next level

Level 3 (Motivated but lacks consistency): **Motivational Intensification**

- Constant appreciation
- Big rewards for little changes
- Joining a regular sports program of interest
- Set qualitative goals
- Break the goals into sub-goals
- Install activity tracking apps
- Keep a positive environment

the problem. Trying to set motivational goals without knowing the mental status of the child may lead to early termination or inadequate treatment outcomes.[5] So, it's a prerequisite to depict the level of motivation needed by a particular child and to trigger the spark within the child's mind, as summarized in Table 1.

Level 1: Motivational Interviewing

At this level, the child has no insight about his/her problem as well as associated repercussions. The major purpose of a health care professional at this level is to educate the children about their current level of health and to counsel them regarding the need to bring a change. It is efficiently done by applying the tool of *Motivational Interviewing*, an empathic person-centered counseling approach that prepares people for change by helping them resolve ambivalence, enhance intrinsic motivation and build confidence to change.[6]

- *Being compassionate* and maintaining a level of *understanding* is the key. "How you discuss a child's weight problem can make a huge difference in helping her deal with it," says Jamie Calabrese, MD, Medical Director of the Children's Institute in Pittsburgh and a member of the American Academy of Pediatrics (AAP) Task Force on Obesity.[7]
- The first encounter of a primary care physician with such a child should just be an attempt to *engage him/her in the conversation, with empathy*. "Can we take a few minutes to discuss your growth in terms of weight and height?" "Well, you are doing good. I want to know your opinion about your own weight and height."
- While questioning, following terms should be avoided and *replaced with less hurting words*:
  - Overweight/obese/heavy/fat: use 'unhealthy weight' instead.
  - Focus on your 'weight': use focus on your 'lifestyle' instead.
  - Junk food/bad food: use 'unhealthy food' instead.
  - Physical exercise: use 'activity/play' instead.
- *Parents should be counseled* to avoid using discouraging words to the child at home to prevent the onset of doubts on his/herself-image.
- Once an insight about the condition has been inculcated into the child's mental milieu, he/she can then be given an appointment for instilling the seed of motivation.

Level 2: Motivational Induction

At this level, the children probably have appropriate insight and know all the answers to the question 'what all is to be done to lose weight and stay fit?' But they are not convinced enough to apply those techniques in daily life. The following tips, to be executed by the parents, are effective in motivating their children towards a healthy lifestyle.

- ***Mindful conversation*:**[8] Girls may be more interested in hearing how lifestyle changes will improve their appearance. Tell your daughter how shiny her hair will look if she eats more fruits and vegetables. Or say, "If you keep playing outdoor games, you'll get into better shape, and we'll probably need to go shopping for some new clothes." Instead of saying, "You are obese and need to lose weight," say "I know you don't like being heavier than your friends. But you can change that by spending less time sitting around and more time moving your body."

- ***Being good role models*:** Physical activity can be inculcated by parents in their children's daily routine by becoming good role models themselves. Scheduling outdoor times with the child like park outings, family walks as well as being active indoors like by asking for help in household chores as per feasibility, dancing sessions, playing ball game, joining swimming classes, etc., are some of the ways parents can accompany the child.
- Assign a time slot as ***'activity hour'* in an *'activity area'*** of the house like a backyard or a balcony or an outside park in the society and ensure that everyone must do some activity or the other during that 1 hour. Playing a family game together can also be another way to spend the 'activity hour'. This would provide an extra edge to parents to interact with their children. They must take advantage of this time to explain the importance of physical activity to the child. However, they should avoid talking about losing weight. Just helping them understand that moving their body would help them feel better in other aspects of life, is enough.
- ***Being sneaky*:** Parents are the mastermind of their children's health as they can adopt sneaky ways to get them active without them realizing that they have been doing it. For e.g., parking the car far away from the exact destination, allotting them the task of taking the dog out for a walk, encouraging them to ditch the elevators by challenging them with stair climbing race, taking a walk to the nearby market instead of reaching there in the comfort of a vehicle, spending the weekend at a trampoline park or kids-friendly trek expedition rather than at a movie or a brunch, encouraging indoor movements by involving them in household chores of their interest, etc. For younger children, they can buy toys that promote physical activity. The key is to stick to the plan and to keep executing such movement-focused ideas. Gradually, the child will develop a habit to stay active without even realising it.
- ***Screen time reduction hacks*:** Tricky ways to reduce screen time in children are removing televisions and computers from their bedrooms, assigning screen-free zones at certain areas of the house like dining area, bedroom, balconies and lawns, and by replacing pre-sleep gadget time with a pre-sleep family fun time as a daily ritual.
- ***Healthy food hacks*:** Taking advantage of the essence of patriotism, the concept of tricolor in Indian flag can be used in meals as well. They can offer a plate containing Indian flag colors. The child might consume it with full interest. At least one meal a day should be planned as a family mealtime as controlling the potion size becomes easier. The rule of 'self-service' should be followed by everyone during the mealtime rather than serving the meals on the table. It's a good idea as well to reserve smaller colorful plates for the child. One should never forget to unstock sweetened beverages and processed foods from the house. Children should accompany the parents to the grocery shopping at least once in a fortnight where they can explore various healthy options available. Involving the children in cooking process as well, inculcates a sense of respect for the food.

Once the goal of induction of motivation has been achieved, move on to the next level.

Level 3: Motivational Intensification

Performing well at this level is the hardest part of the mission for health care professionals as well as parents. The child was motivated enough initially, but the spark usually declines after a week or two. Keeping in mind, the recommendations for an effective activity period of at least 60 minutes a day in order to lose weight significantly, it is imperative to keep that spark alive for a longer period.

- ***Constant appreciation*** for as little endeavors as a 5-minute activity, is a strong driving force for them. A word or two of appreciation from the relatives as well, is enough for them to get going.
- ***Little changes and big rewards*** strengthen their tendency to persevere. Well, it's important to remember not to give junk foods like candies, chocolates, ketchups, fries, pizza or carbonated beverages as rewards. Additionally, reward must not include extra TV time or video game bonanza or a movie date. The best of rewards would be going for a joyful picnic, taking them to an adventure park, buying them a pair of roller skates or a cricket set or a tennis racket, gifting them a Fitbit smart watch that can track their daily steps. Girls have a special predilection for their favorite dress, beautiful hair accessories, a nice pair of shoes, etc.
- ***Joining a regular sports activity*:** Once the child develops a habit of being active throughout the day, which usually happens in a month or so, he would like to join a regular physical activity such as any sports of interest, daily swimming classes, aerobics, etc. One should keep the goals modest

at first, so he/she does not think of exercise as a chore or punishment. Looking at the numbers on the weighing machine as a criterion for achieving the goals can give rise to demotivation as the process is very gradual.

- ***Set qualitative goals*** like fitting into their favorite dress, completing one round of park without getting tired, climbing the stairs in one go, rope skipping for 5 to 10 continuous minutes.
- ***Break down the goals*** further into smaller and more achievable sub-goals. Even a slight progress should be taken as an achievement and celebrated. Seeing progress is a great motivator in itself, and improves self-esteem of the child. Parents should continue to set new goals every month and let the child tackle one goal at a time so that he/she doesn't feel overburdened. Keeping the momentum, helps it feel more automatic over time.
- ***Keep a positive environment*** in the family and encourage the child to have *positive self-talks* like 'I am the best' or 'I am doing great'.
- ***Activity-tracking apps*** can be installed in parent's mobile phone to keep a record of their children's activity. The improvement in their fitness scores calculated by such apps is an excellent motivator.

Rightly said by Karen Salmansohn – "Don't wait until you reach your goal to be proud of yourself. Be proud of every step you take." So, parents must make their child feel proud of every small step they take every day.

SUMMARY

A motivational and autonomy-enhancing approach to behavioral family-based pediatric obesity treatment is a viable alternative to the standard intervention approach.[9] For motivation to be effective, one must proceed at a slow and steady pace taking the child's frame of mind into consideration. Applying the various motivational approaches in a phased manner as depicted above, an obese unmotivated child can evolve into a motivated, activity-conscious, goal-oriented child.

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Study Reveals that COVID-19 Vaccines Lag in Rural, Underdeveloped Areas

According to the study published in the *Lancet Regional Health*, wide disparities in health care coverage, particularly in rural areas, hampered vaccination efforts during the COVID-19 pandemic. In the study, Dr Diego Cuadros, an epidemiologist from the University of Cincinnati, investigated the disparities in vaccination rates across 2,417 US counties. The findings of his study showed that the availability of health care resources influences vaccine coverage. He revealed that barriers to health care access include cost, insurance coverage and transportation. Dr Cuadros concluded that these disruptions were not uniform across the United States, as many counties, especially those in rural areas, experienced significant disruptions in health care, including the distribution of the COVID-19 vaccine itself.

The analysis also revealed that people in underserved communities were as much as 34% less likely to be vaccinated against COVID-19. These included counties in Nevada, Montana, North Dakota, South Dakota and Nebraska where vaccination rates were lowest. (*Source: https://theprint.in/health/covid-19-vaccines-lag-in-rural-underdeveloped-areas-study/1267241/*)

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BRIEF COMMUNICATION

Glucometric Guardianship

SANJAY KALRA*, NAVNEET AGRAWAL†, NITIN KAPOOR‡, ATUL KALHAN#, JOEL TEELUCKSINGH$, RAKESH SAHAY¥

ABSTRACT

This communication conceptualizes, defines and describes glucometric guardianship, as a means of ensuring optimal glycemic management. We define glucometric guardianship as the process of ensuring appropriate measurement, monitoring and analysis of glucose levels, so as to ensure alertness in glycemic management, and agility in anticipating and detecting suboptimal glycemic parameters, and responding to them. This paper hopes to draw attention to the need for glucometric science, encourage debate and discussion and facilitate research on the topic.

Keywords: Capillary glucose, glucose monitoring, indoor glucose management

Modern medical practice is characterized by ever increasing complexity. This is especially true for diabetes care, where a wide spectrum of causative factors, clinical presentations and course of illness, complications and comorbidities intersects with an equally vast offering of therapeutic choices.

The permutations and combinations available to the practicing clinician can be put to efficient and effective usage only if our monitoring systems and strategies are robust. While there are well-developed algorithms for glycemic management in indoor and outdoor settings,[1,2] they do not integrate the nuances of glucose monitoring. Glucometric measurement and analysis is the limiting factor for, and also the stepping stone to, optimal glycemic control. Standardization of glucometrics[3,4] can help improve the process of drug choice and dose titration.

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STEWARDSHIP IN SCIENCE

The concepts of antibiotic stewardship, insulin stewardship and steroid stewardship serve to ensure safe and rational usage of these drugs.[5-7] These campaigns have contributed to greater awareness about the use of these intervention. We propose a similar framework, glucometric guardianship (GG), to highlight the need for systematic use of glucose monitoring devices, in order to accomplish accurate glycemic analysis, optimal glucose control, and comprehensive overall management.

DEFINITION

We define GG as the process of ensuring appropriate measurement, monitoring and analysis of glucose levels, so as to ensure alertness in glycemic management as well as agility in anticipating and detecting suboptimal glycemic parameters, and responding to them. Glucometrics has been defined earlier as the systematic analysis of inpatient glucose data.[8] The authors have called for consensus and standardization so that inter-institutional benchmarking can occur. However, the concept of GG extends far beyond this (Table 1).

The concept of GG encompasses the physical and electronic infrastructure, as well as the human resources involved in glucose monitoring, analysis and management. Infrastructure includes both hardware (glucose measuring devices and ancillary supplies) and software (data recording and analysis) related to glucometrics. Educated and experienced human resources are essential for glycemic management, and GG delineates the roles and responsibilities of various members of the health care team. GG can be used in

Table 1. Domains of Glucometric Guardianship

Equipment

- Choice of glucose monitoring device: e.g., glucometer vs. flash glucose monitoring device; glucometer/FGMS model
- Individual device or common device: e.g., prefer individual glucometer if expected hospital stay of >2-3 days, or if expected number of glucose pricks is >20
- Glucose sticks: available at bedside/central station
- Lancets: available at bedside/central station
- Alcohol swabs: available at bedside or central station
- Meter calibration: needed/not needed and at what frequency

Roles and responsibilities

- Glucose monitoring: by -
- Data entry: by -
- Analysis: by -
- Disposal of used ancillary supplies: by -, at -
- Red flag range: e.g., call duty doctor if plasma glucose <40 mg/dL and >400 mg/dL; check urine/blood ketones if BG >400 mg/dL
- Treatment/titration: by -
- Meter calibration: by -

Patient-specific glucometric guardianship

- Frequency of monitoring
- Site of prick; rotation of fingers
- De-escalation of frequency of monitoring: e.g., if BG 100-200 mg/dL; <20% change in consecutive glucose values at current frequency
- Escalation of frequency of monitoring: e.g., if BG <100 or >200 mg/dL; >20% change in consecutive glucose values

every health care setting: outdoor, indoor and critical care, irrespective of the level of resource availability or allocation.

SUMMARY

Through this communication, we attempt to create a framework for GG in the indoor care setting. This framework can be used as a foundation to create customized GG protocols for every health care setting. It can be modified to suit needs of individual patients as well. The check list format allows for error-free, efficient, user-friendly incorporation into pre-existing standard operating procedures. GG does not replace, but rather complements the algorithms that are already being used by various hospitals.

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BRIEF COMMUNICATION

Heart Smart Diabetes Care

RAKA SHEOHARE*, NAVNEET AGRAWAL†, ASHISH SAXENA‡, SANJAY KALRA#

ABSTRACT

The world is growing smarter day by day, and so is health care. In spite of innumerable inventions and tech-tools, however, we struggle to contain chronic illnesses like diabetes and heart disease. We need to work together and design a rational, scientific and socially sustainable Heart Smart diabetes care ecosystem, with Heart Smart management strategies, to ensure happiness and harmony in persons who live with diabetes.

Keywords: Common soil hypothesis, cardio diabetes pharmacovigilance, Heart Smart diabetes care, ecosystem, rational polypharmacy, total health

Diabetes and cardiovascular disease are two major public health challenges, which are closely linked with each other. Both syndromes have similar risk factors and etiopathological characteristics. Both may present together, and influence each other's clinical features, natural trajectory and choice of treatment. This is why cardiovigilance is an integral part of diabetes care.[1] Modern guidance, in fact, uses cardiovascular status as a primary tool in decision making for glucose-lowering therapy.[2]

Ongoing research and development have led to a greater understanding of the common soil hypothesis, and pathophysiology of both diabetes and cardiovascular disease. Coupled with the greater availability of diagnostics, drugs and devices, this calls for a Heart Smart approach to diabetes care. This review discusses the various aspects of Heart Smart management, in persons living with diabetes.

DIAGNOSTICS

Regular screening for cardiovascular risk factors and surrogate markers is embedded in diabetes care. International recommendations list the questioning and tests that should be carried out at diagnosis of diabetes, and during follow-up. These include lifestyle modification and cessation of tobacco use, targeted control of blood pressure and lipids, along with selective use of antiplatelet drugs.[3]

Recently, N-terminal pro-B-type natriuretic peptide (NT-proBNP) has been approved as a tool for risk stratification in persons with type 2 diabetes.[4] High levels of NT-pro BNP (>125 pg/mL), in asymptomatic persons with type 2 diabetes, suggest a higher risk of heart failure in future. Prescribing annual NT-proBNP and instituting appropriate therapy is an effective, Heart Smart way of preventing hospitalization for heart failure.

DRUGS FOR GLYCEMIC MANAGEMENT

Multiple drugs, belonging to varied drug classes, are available for the management of diabetes. Heart Smart glucose control can be achieved by using glucagon-like peptide-1 receptor agonists (GLP-1RA) and/or sodium-glucose co-transporter 2 inhibitors (SGLT2i) as first-line therapy, along with metformin. Drugs which are proven to have cardiovascular benefit, such as dulaglutide, liraglutide, semaglutide, empagliflozin and dapagliflozin, should be preferred.[2]

DUE DILIGENCE

Cardiovascular health should be monitored while managing diabetes.[1] Tachycardia with GLP-1RA edema with pioglitazone, and postural hypotension with SGLT2i should be looked for, as a part of Heart Smart cardiovigilance. One should also be aware of the overlap between symptoms of hypoglycemia and angina equivalents.

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DYNAMIC CARDIOPROTECTION

The management of diabetes is not limited to glycemic control alone. It includes comprehensive cardiovascular protection, encompassing weight control, lipid-lowering and antiplatelet therapy as required.[3] The World Health Organization (WHO) has set a target of statin coverage for at least 60% of all persons aged >40 years, by the year 2030.[5] Equal, if not more, emphasis should be laid on blood pressure-lowering, achievement of lipid targets and cessation of smoking, to attain optimal cardiovascular protection.

DRUG-DRUG INTERACTIONS

Person living with diabetes are often exposed to polypharmacy, and the inherent dangers of drug-drug interactions. Many drugs used in diabetes praxis may lead to QT prolongation and precipitate arrhythmias. A Heart Smart approach to diabetes care includes 'electrovigilance',[6] so as to minimize the risk of cardiac condition defects and pharmacovigilance, so as to avoid drug-drug interactions.

DUAL RESPONSIBILITY: DIRECT COMMUNICATION

Persons living with diabetes, especially those with cardiovascular disease, often seek treatment from multiple health care providers. There is always a chance of miscommunication and improper prescription, which can be avoided by direct communication between various specialists. A Heart Smart diabetes care program should ensure that specialists' prescriptions, if any, are collated into one complete document and audited to remove dual prescriptions (of antiplatelet drugs, lipid-lowering agents and SGLT2i, for example). Polypharmacy should be rationally prescribed, justified by evidence, backed by pharmacovigilance and based on scientific principles. Referral to superspecialists should be done in a timely and efficient manner whenever needed.

DEDICATION AND PURPOSE

The aim of diabetes management is to ensure a state of sustained comprehensive health, including cardiovascular health. This can be accomplished by creating a Heart Smart diabetes care ecosystem.[7] Such an ecosystem should promote public awareness about the importance of heart-friendly behaviors, and encourage advocacy and action by creating public health programs geared towards Heart Smart diabetes care. The Heart smart ecosystem should welcome and include mental health experts, nutritionists, physiotherapists, yoga experts, sports enthusiasts, gym and sports coaches, along with creative arts experts, apart from clinical specialists.

Diabetes care professionals should be energetic and enthusiastic enough to incorporate nonpharmacological and pharmacological interventions, targeted at cardiovascular health optimization, in their practice. Once these aspects are taken care of, diabetes care will certainly become Heart Smart.

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Law on Euthanasia in India

Life and death as concepts have invited many thinker, philosopher, writer and physician to define or describe them. **Swami Vivekananda** expects one to understand that life is the lamp that is constantly burning out and further suggests that if one wants to have life, one has to die every moment for it. One may like to compare life with constant restless moment spent in fear of extinction of a valued vapor; and another may sincerely believe that it is beyond any conceivable metaphor. Death is complicated and life is a phenomenon which possibly intends to keep away from negatives that try to attack the virtue and vigor of life from any arena. In spite of all the statements, references and utterances, be it mystical, philosophical or psychological, the fact remains, at least on the basis of conceptual majority, that people love to live – whether at eighty or eighteen – and do not, in actuality, intend to treat life like an—autumn leaf.

The perception is not always the same at every stage. There comes a phase in life when the spring of life is frozen, the rain of circulation becomes dry, the movement of body becomes motionless, the rainbow of life becomes colorless and the word life, which one calls a dance in space and time becomes still and blurred and the inevitable death comes near to hold it as an octopus gripping firmly with its tentacles so that the person shall rise up never.

The **ancient Greet philosopher, Epicurus,** has said, although in a different context:

> *Why should I fear death?*
>
> *If I am, then death is not.*
>
> *If death is, then I am not.*
>
> *Why should I fear that which can only exist when I do not?*

But there is a fallacy in the said proposition. It is because mere existence does not amount to presence. And sometimes, there is a feebleness of feeling of presence in semi-reality state when the idea of conceptual identity is lost, quality of life is sunk and the sanctity of life is destroyed and such destruction is denial of real living.

The society at large feels that a patient should be treated till he breathes his last breath.

Every doctor is supposed to take a specific oath that he will make every attempt to save the life of the patient whom he/she is treating and who is under his/her treatment. This oath, thus, puts a moral and professional duty upon a doctor to do everything possible, till the last attempt, to save the life of a patient.

The **Medical Council of India (MCI) Code of Ethics Regulations rejects Euthanasia** (deliberately ending a patient's life at his or her own request or at the request of close relatives). *"6.7* ***Euthanasia: Practicing euthanasia shall constitute unethical conduct****. However, on specific occasion, the question of withdrawing supporting devices to sustain cardiopulmonary function even after brain death, shall be decided only by a team of doctors and not merely by the treating physician alone. A team of doctors shall declare withdrawal of support system. Such team shall consist of the doctor in-charge of the patient, Chief Medical Officer/Medical Officer in-charge of the hospital and a doctor nominated by the in-charge of the hospital from the hospital staff or in accordance with the provisions of the Transplantation of Human Organ Act, 1994."*

While MCI Code of Ethics rejects euthanasia, it does not talk about **physician-assisted-suicide** (where a physician deliberately enables a patient to end his or her life by prescribing or providing medical substances with the sole intent of causing death. But practically, it is included in the same as both acts are contrary to the ethics of medicine and the role of the physician.

Medical scientists have been, relentlessly and continuously, experimenting and researching to find out better tools for not only curing the disease with which human beings suffer from time to time, noble attempt is to ensure that human life is prolonged and in the process of enhancing the expectancy of life, ailments and sufferings there from are reduced to the minimal. There is, thus, a fervent attempt to impress the quality of life.

It is this very advancement in the medical science which creates dilemma at that juncture when, in common perception, life of a person has virtually become unlivable but the medical doctors, bound by their **Hippocratic Oath and medical ethics** want to still spare efforts in the hope that there may still be a chance, even if it is very remote, to bring even such a person back to life.

The Hippocratic Oath taken by a doctor and the MCI Code of Ethics may make him feel that there has been

a failure on his part and sometimes also make him feel scared of various laws. There can be allegations against him for negligence or criminal culpability.

No physician should be forced to participate in euthanasia or assisted suicide, nor should any physician be obliged to make referrals to this end. However, **the right to decline medical treatment is a basic right of the patient.**

The physician does not act unethically in **respecting the patient's wish** to decline medical treatment, even if such a wish may result in the patient's death by allowing the natural dying process to unfold in the course of terminal phases of sickness.

A doctor has a crucial role to play in such situations as there is a very thin line between this ethical and unethical act.

Remember, it is the patient who has a right to deny the treatment and not the relatives. However, the patient must be in his or her sound state of mind to take any such decision.

There is a **distinction between the administration of lethal injection or certain medicines to cause painless death and non-administration of certain treatment,** which can prolong the life in cases where the process of dying that has commenced is not reversible or withdrawal of the treatment that has been given to the patient because of the absolute absence of possibility of saving the life. To explicate, the first part relates to an overt act whereas the second one would come within the sphere of informed consent and authorized omission. The omission of such a nature will not invite any criminal liability if such action is guided by certain safeguards. The concept is based on nonprolongation of life where there is no cure for the state the patient is in and he, under no circumstances, would have liked to have such a degrading state.

In the landmark judgment **Common Cause versus Union of India, 2018 (5) SCC 1, the Hon'ble Constitution Bench of 4 Judges of Supreme Court** held that **Euthanasia** is basically an intentional premature termination of another person's life either by direct intervention **(active euthanasia)** or by withholding life-prolonging measures and resources **(passive euthanasia)** either at the express or implied request of that person **(voluntary euthanasia)** or in the absence of such approval/consent **(non-voluntary euthanasia)**.

Active euthanasia also includes physician-assisted suicide, where the injection or drugs are supplied by the physician, but the act of administration is undertaken by the patient himself. Active euthanasia is not permissible in most countries.

Passive euthanasia is when medical practitioners do not provide life-sustaining treatment ((i.e., treatment necessary to keep a patient alive) or remove patients from life-sustaining treatment. This could include disconnecting life support machines or feeding tubes or not carrying out life-saving operations or providing life-extending drugs. In such cases, the omission by the medical practitioner is not treated as the cause of death; instead, the patient is understood to have died because of his underlying condition.

Further, in **Gian Kaur versus State of Punjab, (1996) 2 SCC 648**, the Hon'ble Constitution Bench of Apex Court expounded that the word **"life" in Article 21** has been construed as life with human dignity and it takes within its ambit the **"right to die with dignity"** being part of the **"right to live with dignity"**. As part of the right to die with dignity in case of a dying man who is terminally ill or in a persistent vegetative state, only passive euthanasia would come within the ambit of Article 21 and not the one which would fall within the description of active euthanasia in which positive steps are taken either by the treating physician or some other person. That is because the right to die with dignity is an intrinsic facet of Article 21.

In **Aruna Ramachandra Shanbaug versus Union of India, 2011 (15) SCC480**, Hon'ble Supreme Court has observed that **autonomy means the right to self-determination where the informed patient has a right to choose the manner of his treatment.** To be autonomous the patient should be competent to make decisions and choices. In the event that he is incompetent to make choices, his wishes expressed in advance in the form of a Living Will, or the wishes of surrogates acting on his behalf ('substituted judgment') are to be respected.

Thus, **all adults with the capacity to consent have the common law right to refuse medical treatment and the right of self-determination.** Doctors would be bound by the choice of self-determination made by the patient who is terminally ill and undergoing a prolonged medical treatment or is surviving on life support, subject to being satisfied that the illness of the patient is incurable and there is no hope of his being cured.

In "**Common Cause versus Union of India, 2018 (5) SCC 1** the Constitution Bench of Hon'ble Supreme Court held that **Advance Medical Directive** would serve as a fruitful means to facilitate the fructification of the sacrosanct right to life with dignity. The said

directive will dispel many a doubt at the relevant time of need during the course of treatment of the patient. That apart, it will strengthen the mind of the treating doctors as they will be in a position to ensure, after being satisfied, that they are acting in a lawful manner. However, Advance Medical Directive cannot operate in abstraction. The Hon'ble Court in the said judgment has enumerated various safeguards and procedure of advance medical derivatives and also in cases where there is no advance medical derivatives which will remain enforced till Parliament makes a law on Advance Medical Derivatives.

■■■■

Characterization of Risk Factors for Sudden Infant Deaths

Infants who sleep on a nonapproved sleep surface and use soft bedding are at a considerably high risk of explained suffocation, according to a study published online December 5, 2022 in the journal *Pediatrics*.[1]

This study sought to explore the risk factors for sleep-related suffocations and unexplained infant deaths (including deaths due to sudden infant death syndrome [SIDS]) together grouped as sudden infant deaths. For this, the researchers analyzed data from the Sudden Unexpected Infant Death (SUID) Case Registry of the Centers for Disease Control and Prevention (CDC) data, from 2016 to 2017. Live born infants from the Pregnancy Risk Assessment Monitoring System (PRAMS) constituted the control group. The age group of the infants included in the study was 2 to 9 months; 300 unexplained infant death cases with 1,200 age-matched controls and 112 sleep-related suffocation cases with 448 age-matched controls.

Among infants who did not share a room with their mother or caregiver, the risk of sleep-related suffocation was increased by almost nineteenfold with adjusted odds ratio (aOR) of 18.7. They were also nearly 8 times more at risk of unexplained death with aOR of 7.6 compared with infants who shared a room. Infants who shared their sleep area with their pet/toys or another person also doubled their risk of sleep-related suffocation or unexplained infant death with aORs of 2.5 and 2.1, respectively.

Infants who slept in a nonsupine (not on back) sleep position were nearly 2 times more likely to experience sleep-related suffocation and unexplained death with aORs of 1.9 and 1.6, respectively.

The risk of explained suffocation increased 16 times among infants who slept on a soft bedding such as loose bedding, stuffed toys and other objects close by (aOR 16.3) than in those who did not sleep on soft bedding. The risk of unexplained death was also increased among these infants (aOR 5.0). Infants who did not sleep in a crib, bassinet or portable crib were 4 times more at risk of explained suffocation death versus infants who slept on a firm and noninclined sleep surface (aOR 3.9). No such association was observed for unexplained sleep death in this group of infants (aOR 1.0).

This study has reiterated the association of unsafe infant sleep practices and sleep-related suffocation and unexplained infant death. It has also characterized the risk factors separately for sleep-related suffocation and unexplained infant death. Infants who slept alone were at the highest risk, almost 20 times higher, of sleep-related suffocation and unexplained infant death. Nonapproved sleep surface was strongly associated with explained suffocation, but not with unexplained sleep death. Use of soft bedding had a stronger association with suffocation than unexplained death.

In its updated 2022 recommendations for reducing infant deaths in the sleep environment, the American Academy of Pediatrics (AAP) recommends use of a firm, noninclined sleep surface, supine positioning, avoidance of soft bedding, room sharing without bed sharing and overheating.[2]

By highlighting the associated dangers, the findings of this study can be used by pediatricians to educate parents about safe sleep.

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HCFI Dr KK Aggarwal Research Fund

Coronavirus Updates

China eases COVID restrictions

In a major shift from its zero COVID policy, China has now allowed home quarantine for asymptomatic cases and patients with mild COVID-19. These patients can shift to designated hospitals if their condition worsens, according to the National Health Commission (NHC). The policy regarding high-risk zones has also changed. Now the high-risk areas will be defined by "building, unit, floor and household" and not the entire buildings or residential societies… (*Source: Medscape, Dec. 8, 2022*)

Children aged 6 months are now eligible for COVID vaccine

The US Food and Drug Administration (FDA) has authorized the bivalent Pfizer-BioNTech and Moderna COVID-19 vaccine for emergency use in children as young as 6 months of age. Now children aged 6 months to 5 years, who have been vaccinated with the monovalent Moderna vaccine can now take the single dose of bivalent vaccine as booster after a gap of 2 months. While the unvaccinated children in the age group 6 months to 4 years will get the bivalent Pfizer vaccine as the third dose after two doses of the original Pfizer vaccine…(*Source: US FDA, Dec. 8, 2022*)

Effectiveness of COVID-19 vaccines against long COVID

Compared to the unvaccinated, even a single dose of the vaccine was protective against long COVID. Analysis of data of 1.6 million subjects showed that the effectiveness of a single dose of Pfizer, Moderna, AstraZeneca or the J&J vaccine in preventing long COVID ≥3 weeks was 29%. The protective efficacy increased to 35% among individuals who had taken the vaccine prior to getting COVID-19 compared to 27% effectiveness in those who took the vaccine post-COVID-19… (*Source: Antimicrobial Stewardship & Healthcare Epidemiology, Dec. 6, 2022*)

Marked increase in suicidal ideations during the pandemic

A *PLoS One* study has reported almost fivefold increase in suicidal ideation during the COVID-19 pandemic. A 13% increase in suicidal ideation was noted in the study. Thirty-one percent of people who were unable to pay rents developed suicidal ideation, while 24% of those who lost their jobs and 25% of those who were lonely had high prevalence of suicidal ideation… (*Source: PLoS One, Nov. 16, 2022*)

Benefits of COVID-19 vaccine in patients with rheumatic disease

Fully vaccinated patients with rheumatic disease reduce their chances of developing long COVID by at least 50%. Four weeks post-COVID, 41% of the fully vaccinated patients reported at least one symptoms versus 54% of the partially or unvaccinated patients. After 3 months, 21% of fully vaccinated patients complained of one persistent symptom compared with 41% of the partially or unvaccinated patients… (*Source: Annals of Rheumatic Diseases, Nov. 28, 2022*)

WHO Director General hopes to remove the global public health emergency tag from COVID-19 next year

Addressing a media briefing, Dr Tedros Ghebreyesus, WHO Director General expressed hope that the COVID-19 pandemic would not be considered a global public health emergency in the coming year. When quizzed about the conditions for lifting the Public Health Emergency of International Concern (PHEIC), WHO's Senior Epidemiologist Maria Van Kerkhove said that there's more work to be done… (*Source: Medscape, Dec. 15, 2022*)

Hong Kong permits 5th COVID-19 dose

Following a resurgence in COVID-19 cases, the government of Hong Kong has allowed the residents aged 18 years to take a 5th dose of the COVID-19 vaccine… (*Source: Reuters, Dec. 16, 2022*)

Hong Kong lifts restrictions for international visitors, but testing on arrival stays

Hong Kong has ended the "amber" health code for international visitors to the city. Inbound travelers, testing negative on polymerase chain reaction (PCR) COVID test on arrival, can now freely visit the restaurants, gyms and other venues as soon as they land in the city. Undergo the "0 + 3" medical surveillance period is no longer mandatory. However, a vaccine certificate is still required. Residents also do not need to scan QR codes with the mandatory "Leave Home Safe" app… (*Source: Lifestyle Asia, Dec. 13, 2022*)

China has stopped including asymptomatic cases in its daily COVID cases count

From 14th December, China will not include new asymptomatic infections in the total count of COVID-19 cases. According to the NHC, many asymptomatic cases do not undergo testing leading to an inaccurate number of cases. Till now, China had counted symptomatic and asymptomatic infections separately… (*Source: Medscape, Dec. 14, 2022*)

Travelers to Nigeria no longer need to undergo COVID testing

International travelers to Nigeria will not be required to undergo testing for COVID-19 regardless of the vaccination status. Also, it is not mandatory to wear masks inside the flights and inside the airport. However, travelers aged 60 years and above and those with underlying medical conditions are encouraged to wear face masks… (*Source: Medscape, Dec. 14, 2022*)

COVID-19 vaccines have saved more than 3 million US lives, says study

A study released by the Commonwealth Fund has found that COVID-19 vaccines prevented more than 120 million more infections, more than 18.5 million additional hospitalizations and 3.2 million additional deaths from December 2020 through November 2022. Vaccines also saved at least one trillion US dollars in health care costs… (*Source: The Commonwealth Fund, Dec. 13, 2022*)

Bharat Biotech's intranasal COVID vaccine gets approval as booster

Incovacc, the intranasal COVID-19 vaccine from Bharat Biotech has been granted approval for restricted use in adults aged ≥18 years to be administered as a booster dose through nasal drops. It may be introduced in the CoWin platform. For now, the intranasal vaccine will be available in private hospitals. It is the first intranasal vaccine to get approval both as primary series and heterologous booster vaccine… (*Source: Times of India, Dec. 23, 2022*)

China faces a humongous surge in COVID-19

Hospitals in China are apparently becoming overwhelmed with a surge in infections amidst a new Corona wave in the country, according to the WHO, although the official figures appear to contradict this. The numbers have been rising since the stringent restrictions that had been in place as part of the country's zero COVID policy were eased a fortnight back. The elderly population is especially vulnerable… (*Source: BBC, Dec. 22, 2022*)

"Very concerned" about COVID situation in China, says WHO Director General

Dr Tedros Ghebreyesus, WHO Director General has said that the WHO is "very concerned" about the rising reports of severe COVID-19 across China after it lifted many measures under its zero COVID policy. The low vaccine uptake has also put a large population at risk of getting the infection. Recently, a press briefing on 21st December, he said that the WHO needs more information about hospitalizations including ICU admissions "to make a comprehensive risk assessment of the situation on the ground"… (*Source: Associated Press, Dec. 21, 2022*)

Decline in active cases in the country

India recorded 163 new COVID-19 cases and 9 deaths in the last 24 hours, as per latest data from the Health Ministry. The active case count has now decreased to 3,380 (0.01%). The total number of cases are 4.46 crores and deaths are 5,30,690 (1.19%). The total vaccination has crossed 2.20 crores… (*Source: PTI, Dec. 23, 2022*)

BF.7 variant present in 91 countries since last year

The BF.7, also known as BA.5.2.17, variant has been in circulation since last year and has been detected in 91 countries according to a report by the Scripps Research Institute. It is a sublineage of the Omicron variant. As per the report, the global prevalence of BF.7 has been 0.5% worldwide in sequenced samples. BF.7 is presumed to be the key variant behind the latest surge in cases in China… (*Source: Times of India, Dec. 23, 2022*)

With inputs from Dr Monica Vasudev

HCFI Round Table Environment Expert Zoom Meeting on "Construction and Demolition Waste (C&D Waste) Management: Issues and Challenges – Part 1"

December 4, 2022 (Sunday, 12 noon – 1 pm)

- Construction and demolition (C&D) waste is waste generated from construction activity, renovation, repair and demolition of houses, buildings, roads, bridges, etc.
- The major components of C&D waste are cement concrete (demolished), broken bricks, broken cement plaster, steel, rubble, broken stone, broken timber and wood, soil and sand and gravel. About 70% of C&D waste consists of mixed sand and soil.
- Management of C&D waste particularly in towns and cities is a big challenge. It is generally dumped in landfills, where recycling facilities are lacking. It is also an important source of air pollution,

especially in Delhi-NCR area. Not just air pollution, it is also a concern for land and water pollution too.

- Earlier C&D waste was covered under the then existing Municipal Solid Wastes (Management and Handling) Rules, 2000. In 2016, the MoEF, Government of India notified a separate rule called Construction and Demolition Waste Management Rules, 2016. There rules are applicable to every waste resulting from construction, remodeling, repair and demolition of any civic structure of individual or any organization or authority, which generates C&D waste as building material, debris, etc. In 2017, the Central Pollution Control Board (CPCB) also issued guidelines on the management of C&D waste.
- There is a huge gap between generation and processing or recycling of C&D waste. The waste that is not processed or recycled finds its way either to landfill sites or is dumped in the roadside or flood plain, forest area, drain side.
- The total construction market in India is over Rs. 9,00,000 cr per annum. Construction industry is growing at twice the world average. C&D go side by side; hence, C&D waste is generated. In India, the annual generation of C&D waste in 2018 was 100 million MT of C&D waste is generated. In Delhi, the amount of C&D waste is 7,000 tons/day.
- Metal, wood, plastic are not found in C&D waste. We find soil, sand, aggregates and chips.
- To manage C&D waste it is important to estimate it. Estimation will depend only on the progress of the construction.
- In 2000, TIFAC (Technology Information, Forecasting and Assessment Council) found that for new construction, around 40 to 60 kg/sq. m of C&D waste is generated; for building repair, it is around 40 to 50 kg/sq. m and for demolition of buildings, it is around 300 to 500 kg/sq. m. This needs to be revisited.
- In 2017-18, IIT Kanpur conducted a study where they found that from 7,000 MT waste of Delhi; 6.5 tons/day of PM10 and PM2.5 is generated.
- If C&D waste is properly managed, then up to 95% to 98% can be recycled.
- From C&D waste we get soil, sand, recycled aggregate and recycled concrete aggregate. From these, value-added products like kerb stones, paver blocks, tiles, brick blocks are made nowadays.
- In India, the journey of C&D waste started in 2005. The first plant came up in Delhi at the time of Commonwealth Games in 2009. In 2014, the Indian Concrete Institute (ICI) and the Central Public Works Department (CPWD) together made guidelines for reuse and recycle of C&D waste, from generation to disposal process to use of recycled products. In 2015, UN made a guideline and in 2016, GIZ made another report. The C&D waste management rules were formulated only in 2016 by the government. CPCB made its guidelines in 2017. In the same year, GIZ made training manual for this. In 2018, NITI Aayog made a report. In 2018, the Building Materials and Technology Promotion Council (BMTPC) developed guidelines on C&D waste recycling. After great efforts, in 2016 Bureau of Indian Standards (BIS) incorporated it into IS 383. The specifications and rates have been finalized along with CPWD, but they are not being used.
- The C&D waste management rules are for every individual, local bodies, state governments, bulk waste generators, pollution control boards, CPCB and also for the Central Government.
- The quality of recycled aggregates from mixed C&D waste has been tested for 6 months and was found to be safe.
- In Delhi, out of the 7,000 MT of waste generated, ~6,500 MT is collected per day. Out of this; 5,000 reaches the plants and 1,500 goes to the landfill sites.
- There are collection centers in every ward where small generators can dispose of their C&D waste at designated sites, from there the MCD collects it and takes it to the plants.
- Bulk waste generators directly dispose of the waste at the plants.
- The plant in Shastri Park, Shahdara was started in 2015 with a capacity of 500 tons, now the capacity has increased to 1,000 tons/day. One of the most advanced wet processing technologies has been adopted in this processing facility.
- The first plant in Jahangirpuri began with capacity of 500 MT and was further expanded to 2,000 MT.
- Mundka waste processing facility has processed 1.5 lakh MT of C&D waste since its inception. The Bakkarwala processing facility has processed 2.5 lakh MT of C&D waste since inception.
- So far, these projects have processed around 80 lakhs of C&D waste. The government of India has made it compulsory to install one such plant in cities with a population of above 10 lakh.

- For air quality management, water sprinklers are used during unloading and operations. Recycled water is used for wet processing. Greenery has been developed to attenuate noise.
- If we generate 100 tons waste, from this 50% is soil. Soil and sand can be separated in the plant. Five percent recycled concrete aggregate is recovered; 24% recycled aggregates, 15% manufacturer's sand, 1% to 5% plastic, iron, etc. Value-added produces like bike kerb stones, concrete blocks, brick blocks, paver blocks and tiles are made from this.
- All bus stops in Delhi during Commonwealth Games were renovated with these tiles. All the material used in the new Supreme Court building is from recycled material.
- Processing of the C&D waste is done by using state of the art wet/dry process technology.
- Reuse of C&D waste will reduce burden on dumpsites. City will be cleaner; drain clogging will be less. Useful products made out of recycled waste can be again used by the building industry. It will save natural resources.
- Separation of concrete waste and nonconcrete waste greatly increases financial viability.
- Way forward: Seamless integration from demolition to processing, incentive to waste generator for sale of C&D waste and concession on purchase of recovered material including value-added products.
- The challenges we face are sector-specific and geographic-specific. The enforcement cannot be the same across the country has to be different.
- Forty percent of the total waste in Delhi is C&D waste, which contributes to 650 units of ppm. This needs serious attention as to how strict enforcement right from generation to disposal happens. Proper management of C&D waste may lead to improvement in air pollution with Delhi being an urban island.
- Circularity in waste means where every bit can be reused and recycled for many productive things.
- There are so many constructions going on in Delhi but where the waste goes is not defined. No accountability, no transparency. Data compilation is a big challenge.
- It should not be looked as NIMBY (not in my backyard) factors but as CIMBY (circularity in my backyard) factors. CIMBY has to be practiced in such a way that this particular waste which contributes to 40% of waste in Delhi needs to be returned back to the society. Everything should be highly priced and not be given on discount. People should be given incentives, which can be in the form of tax rebate, enhance FAR, rebate on building fee, etc.
- When the municipal corporation sanctions any building plan then it should put a condition how they will dispose of the C&D waste and how they will comply. Implementation is poor.
- The management at the level of local bodies needs to be strengthened so that all these conditions that are imposed during sanction of plan are really monitored and seen that they are implemented.
- Construction and demolition waste is being dumped in the green belts, where trees and shrubs die with time.
- The products made from C&D waste are good for non-load bearing structures.
- It has been made mandatory for the contractors to at least use 10% of these products in circulatory areas.
- Every department should have an environment department for awareness about the rules, which usually do not percolate down. People should be aware of the repercussions of not following the rules.

Participants: Dr Anil Kumar, Mr Pradeep Khandelwal, Mr Sanjiv Kumar, Dr Sanjeev Agrawal, Mr Neeraj Tyagi, Dr Dipankar Saha, Mr PK Jain, Mr Vikas Singhal, Dr S Sharma

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Diabetes India 2022: 12th World Congress of DiabetesIndia

METFORMIN SUPREME POSITION AS A FIRST CHOICE: PROS AND CONS

Dr Meena Chhabra, New Delhi

Based on the medical community's extensive experience and the drug's demonstrated efficacy, safety and low-cost, metformin should remain the "foundation therapy" for all patients with type 2 diabetes, barring contraindications.

Metformin is contraindicated in:

- Patients with severe renal dysfunction (glomerular filtration rate [GFR] <30 mL/min/1.73 m^2).
- Hypersensitivity to metformin and metabolic acidosis. Metformin dosing should also stop on the day of any surgery.
- Discontinue metformin before giving iodinated contrast agents in patients with a GFR <60 mL/min/1.73 m^2, lactic acidosis risk factors.
- Metformin may be restarted after the procedure once the patient's GFR has normalized. Avoid metformin in hepatically impaired or unstable heart failure patients.
- Sodium-glucose co-transporter 2 (SGLT2) inhibitors or glucagon-like peptide-1 receptor agonists (GLP-1RA) may only be considered as first-line therapy in case of atherosclerotic cardiovascular disease (ASCVD) or high/very high cardiovascular (CV) risk.

RESPONDERS AND NONRESPONDERS TO SGLT2 INHIBITORS AND GLP-1 RECEPTOR AGONISTS: POSSIBLE MECHANISMS AND OPPORTUNITIES

Dr Leszek Czupryniak, Poland

- Aspects of the mechanisms of GLP-1RA-induced weight loss: Weight loss induced by caloric restrictions leads to a compensatory reduction in energy expenditure; Weight loss induced by semaglutide only transiently did so: energy expenditure returned to baseline levels within a week.
- The possible mechanism for (non)-responding to GLP-1RAs are GLP-1 receptor genetic polymorphism, various degrees of receptor response to GLP-1, adaptations in basal metabolic rate, varied CND response to hypothalamus stimulation, early vs. late responders, duration of the history of obesity and increased vs. decreased patient's motivation to lifestyle modification.
- The possible mechanism for (non)-responders to SGLT2 inhibitors is compensatory hyperphagia-varied degree, adaptations in basal metabolic rate and complex hormonal changes due to calorie loss with urine.
- Clinical questions that remain unanswered are: Successful identification of early and late and nonresponders - clinical criteria; Giving up medications in non (late?) responders vs. intensifying therapy; Combination therapy - in whom, in what sequence?

WHAT FUTURE TREATMENTS ARE ON THE HORIZON FOR NAFLD?

Dr Shalini Jaggi, New Delhi

- One in five individuals globally are estimated to have nonalcoholic fatty liver disease (NAFLD). Its prevalence is strongly associated with obesity and metabolic disorders; however, evidence is mounting among nonobese individuals.
- Whilst bland steatosis itself is not harmful, it lays the foundation for the development of nonalcoholic steatohepatitis (NASH) and hepatocellular carcinoma. The complex and heterogeneous nature of NAFLD challenges the quest to find the holy grail of treatments.
- So far treatments are generally aimed at directly ameliorating either one of the hallmark characteristics driving NAFLD (steatosis, inflammation and fibrosis) or the gut microbiome. The NAFLD treatment landscape is rapidly evolving as a consequence of our growing understanding of its underpinning mechanisms. Treatments aimed at ameliorating not one, but multiple, features of the condition hold great promise. Several treatments have been tested in clinical trials, and whilst some promising results have been obtained, most have failed to deliver the desired outcome.

- Increasing appreciation of the heterogeneity of NAFLD will enable us to develop more personalized therapies. Whilst the holy grail has not yet been found; step by step, its quest is ongoing and getting closer to the discovery of successful NAFLD treatments.

ARE WE MISSING EVIDENCE-BASED PRACTICE IN DIABETES?

Dr Benny Negalur, Thane, Maharashtra

If we all agree on best practices based on data and research – we can reduce unnecessary care, save money and push people into pathways to yield better results.

- Scientific discovery in recent years has led to important advances in our understanding of the mechanisms that may underlie type 2 diabetes.
- Interventions to increase exercise, reduce weight and control elevated glycemia, blood pressure (BP) and cholesterol levels demonstrated a significant decrease in morbidity and mortality. Many barriers to the adoption of evidence into clinical care at the community level exist. Diabetes translational issues are diverse and complicated. No single best practice is appropriate for all patients and practitioners. Tailoring to patients and customizing to settings is necessary.
- Real-world translation requires flexibility to deal with pragmatic issues such as provider time constraints, reimbursement and system problems.

DIABETES CARE: TIME TO CONCENTRATE ON COMPREHENSIVE CARE

Dr SR Aravind, Bengaluru

- Diabetes mellitus is one of the most serious chronic illnesses in the world due to its prevalence, economic and social effects, and negative impact on the quality of life of the affected people.
- The diagnosis implies changes in life habits especially related to feeding, physical activity and constant self-care, requiring greater personal autonomy.
- Complications - both microvascular and macrovascular can lead to poor quality of life. Physically, mentally and economically draining leading to both patient and family suffering.
- Mysteries of diabetes are evolving and will continue - continuous knowledge update is a must.
- The failure of clinicians to intensify therapy when clinically indicated has been termed "clinical inertia".
- Education and comprehensive care throughout life are the keys to good health in people with diabetes.
- Education is 'hand holding' the patient for life.
- Diabetes care is teamwork, turning out to be cardiometabolic, renal and vascular in approach.
- The basic minimum care team in diabetes comprises doctors, patients, dieticians, diabetes educators and nurse educators.
- The success of your diabetes management depends on:
  - Guideline-directed medical therapy
  - Evaluate practice pattern, patient segment, and plan the process
  - Evaluate patients for micro- and macrovascular complications
  - Educate each patient, each visit with patience
  - Practice care with empathy - learn soft skills and communication
  - Contribute to research, audit your practice
  - Be accessible-affordable-accountable
  - Never chase success - chase satisfaction.

ARE WE MIGRATING FROM SMBG TO CGM?

Dr Banshi Saboo, Ahmedabad

- Self-monitoring of blood glucose (SMBG) measurements do not capture the post-meal spike while continuous glucose monitoring (CGM) captures post-meal spike and glycemic excursions across the day.
- CGMs provide information about the glucose concentration as well as trend information about the direction and rate of changing glucose concentrations.
- Guidelines recommend the use of CGM in diabetes management.
- Numerous randomized controlled trials have demonstrated benefits from using real-time CGM over SMBG, including a lower A1c and/or reduced hypoglycemia.

FOCUS ON TIR THROUGH CGM TO TARGET BETTER CLINICAL OUTCOMES IN DIABETES

Dr Manoj Chawla, Mumbai

- There are many faces of A1c, though HbA1c is still a standard measure for glycemia, they don't provide a complete picture.

- Ambulatory glucose profile (AGP) carries metrics data of time-in-range (TIR) and is crucial in SMBG, CGM, etc.
- % TIR and HbA1c have a broad correlation between a range of subjects, ages and technologies across 18 subjects.
- For every absolute 10% change in % TIR, there is approximately a 0.8% reduction in HbA1c along with a 6.4% risk reduction for abnormal carotid intima-media thickness (CIMT).
- TIR and glycemic variability (GV) are mathematically interrelated; however, they are not interchangeable.

A SILVER LINING IN THE ARMAMENTARIUM OF DIABETES THERAPY: THE BIRTH OF THE WORLD'S FIRST "PEPTIDE IN A PILL"

Dr Rajiv Kovil, Mumbai

- Peptides are challenging compounds and require engineering to optimize their *in vivo* performance.
- Peptide analogs can be designed to offer improved stability and prolonged $t_{1/2}$, while a formulation approach can facilitate improved absorption.
- Absorption of oral semaglutide takes place in the stomach and requires coformulation with SNAC.
- The mechanism of absorption is shown to be compound-specific, transcellular and without any evidence of an effect on tight junctions.
- The development of "peptide in a pill-oral semaglutide" represents an advancement in treatment possibilities for chronic diseases by transforming injectable therapies into tablet-based oral formulations.

CARDIOVASCULAR OUTCOME TRIAL REQUIREMENTS SHOULD NOT BE ABANDONED

Dr Rajeev Chawla, New Delhi

- The requirement to test one new drug in class should be tested in cardiovascular outcome trial (CVOT) to give assurance and evidence to treating physicians about its efficacy and safety.
- It should be noted that in referring to cardiovascular disease (CVD), we include not only macrovascular but also microvascular morbidity.
- Both are equally important from a CV outcome point of view.
- New and existing glucose-lowering therapies should be evaluated for their overall effects on vascular health, the various CV phenotypes (e.g., heart failure), and specific vascular complications such as amputations.
- CVOTs have sensitized diabetes care providers to the opportunities for multifactorial and comprehensive diabetes care, including CV risk reduction.
- Some of the more recent CVOTs have embraced comprehensive cardiorenal primary endpoints, originally proposed by investigators from earlier trials.
- CVOTs have still a long way to go. Primary intervention trials in lower-risk populations could determine whether diabetes medications offer CV protection for those who do not yet have CVD.

25 YEARS OF ACARBOSE IN INDIA

Dr BM Makkar, New Delhi

- In Indian patients considering a carbohydrate-rich diet, acarbose works by inhibiting alpha-glucosidase causing a delay in intestinal absorption of carbohydrates along with decreasing insulin need.
- The structural uniqueness of the acarbose reduces postprandial plasma glucose (PPG) via an insulin-sparing mechanism and facilitates its entry into the large intestine.
- Several studies have proved that acarbose reduces Hb1Ac by 0.8% along with a reduced risk of progression from prediabetes to type 2 diabetes.
- Acarbose is recommended by various international communities owing to glucose-lowering efficacy across a broad range of patients, regardless of BMI, HbA1c, duration of diabetes, insulin resistance, condition of β cells, age, etc.

DPP-IV AND ORGAN PROTECTION: EVIDENCE-BASED CHOICES

Dr SK Sharma, Jaipur

- Dipeptidyl peptidase-4 (DPP-4) inhibitors beyond its well-established actions on the pancreas GLP-1 further exert direct effects on the heart, vessels and kidneys, mainly via the GLP-1 receptor.
- Preclinical evidence suggests that DPP-4 inhibitors may be beneficial in settings of acute renal failure and chronic kidney diseases (CKDs) such as diabetic nephropathy, but also cardiac diseases such as myocardial infarction and heart failure.
- DPP-4 inhibitors raise the possibility of a direct renoprotective effect independent of improvements in glycemic control.

- DPP-4 inhibitors demonstrate clinically meaningful benefits in clinical phase 3 and 4 trials in the treatment of acute kidney failure, chronic kidney failure and acute myocardial infarction as well as heart failure.

MECHANISM OF β-CELL DYSFUNCTION IN T2DM

Dr Om Lakhani, Ahmedabad

- Over 50% of β-cell function is lost at the time of diagnosis along with a 4% to 5% reduction every year in type 2 diabetes patients.
- Beta-cell impairment is the key to the pathogenesis of type 2 diabetes.
- In comparison to the insulin resistance in a prediabetic patient, diabetic patients have both insulin resistance and β-cell dysfunction as insulin secretion is a cumulative factor of β-cell mass and its function.
- Preservation of β-cell is the key to preventing progression from prediabetes to type 2 diabetes and further disease progression in type 2 diabetes patients itself.

TIMELY INTERVENTION IN T2DM: FOCUS ON SGLT2–DPP-4 INHIBITOR COMBINATIONS

Dr AG Unnikrishnan, Pune

- The sequential treatment approach is often compounded by substantial clinical inertia to timely treatment intensification. Substantial clinical inertia exists at each sequential intensification step.
- At HbA1c 8.0% to 8.5%, HbA1c-lowering is slightly greater with DPP-4 inhibitors than with SGLT2 inhibitors as an add-on to metformin. SGLT2 inhibitors are associated with larger HbA1c levels.
- DPP-4 inhibitors moderate the risk of genitourinary tract infections associated with SGLT2 inhibitors.
- In cases of HbA1c ≥8.0%, dual DPP-4 inhibitors-SGLT2 inhibitors add-on therapy to metformin should be considered to help more patients achieve glycemic targets.
- Real-world evidence with empagliflozin and linagliptin FDC conducted across India involving 1,232 T2D patients showed a significant reduction in HbA1c, fasting plasma glucose (FPG), PPG, weight and BP.

UNLEASHING THE POTENTIAL FOR RENAL PROTECTION WITH SGLT2 INHIBITION: A CLINICAL PERSPECTIVE

Dr NK Singh, Dhanbad

- SGLT2 inhibitors are an important weapon in our arsenal against not only type 2 diabetes but also the conditions that we encounter that go hand-in-hand, including CKD and CVD.
- Frontline clinicians should initiate SGLT2 inhibitors for patients with type 2 diabetes and diabetic kidney disease who have an eGFR of at least 30 mL/min/1.73 m^2.
- Deferring initiation of SGLT2 inhibitors to a specialist (a nephrologist or endocrinologist) will result in a faster progression of diabetic kidney disease irrespective of glycemic control, and it is crucial to initiate these medications as early as possible.
- Prescribers should be aware of the initial reversible drop in eGFR of approximately 5 to 8 mL/min/1.73 m^2 (up to a 20% drop) in the first 2 weeks after starting SGLT2 inhibitors, which is due to the hemodynamic effects of the drug.
- The use of an SGLT2 inhibitor can slow the decline in GFR, reduce the onset of microalbuminuria and slow or reverse the progression of proteinuria.

LATENT AUTOIMMUNE DIABETES IN ADULTS

Dr Sanjay Reddy, Bengaluru

- Latent autoimmune diabetes in adults (LADA), dubbed type 1.5 D may account for 2% to 12% of all cases of diabetes in the adult population.
- LADA is a form of diabetes mellitus that has characteristic manifestations similar to both type 2 diabetes and type 1 diabetes. Early diagnosis is paramount to inhibiting appropriate treatment and preventing complications.
- New insight into the pathophysiology of LADA explained the slow progression of β-cell destruction.
- Insulin, DPP-4 inhibitors alone or in combination with thiazolidinediones, and GLP-1 receptor inhibitors have shown promising results in controlling glycemic levels and preserving β-cell functions.

■■■■

News and Views

Impact of the Color of the Serveware on Taste Perception

The color of the serving plate or bowl affects the perception of the taste of the food, suggests a study from the UK published in the journal *Food Quality and Preference*.[1]

Researchers from the Dept. of Psychology at University of Portsmouth in the UK enrolled 47 individuals to examine if color had any effect on food preferences. The study participants were assigned a questionnaire to measure Food Neophobia (FNS), which is the fear or reluctance of trying new food. Based on their responses they were categorized as picky or fussy eaters and non-picky eaters. They were asked to taste the same food item served in blue, red and white bowls.

Results showed that the color of the bowl affected the saltiness and desirability of the food in the picky eaters. The food served in the red and blue bowls was deemed saltier compared to the food in the white bowl. Food in red bowls rated the least on desirability. No such effects of the color of the bowls were observed among those who were not fussy eaters.

Sense of smell or olfaction and food texture is known to influence food choices or preferences. This study has attempted to decode fussy eating and shown for the first time the association between color of the bowl or plate in which food is served and perception of taste. It is often a struggle to get picky eaters to eat. The findings of this study possibly show a way out to deal with fussy eating.

Reference

1. Madison A, et al. How colour influences taste perception in adult picky eaters. Food Qual Prefer. 2023;105:104763.

Cervical Polyps: A Risk Factor for Spontaneous Preterm Labor?

The risk of spontaneous preterm labor is increased fourfold in pregnant women diagnosed with cervical polyp in the first trimester of pregnancy and which are not removed compared to women without polyps, suggests a recent study published in *The American Journal of Obstetrics and Gynecology*.[1]

In this study, researchers from the Osaka Women's and Children's Hospital in Osaka, Japan retrospectively analyzed medical records of 4,172 pregnant women at less than 12 weeks of gestation between January 2015 and December 2019. These participants had been detected to have cervical polyp on routine vaginal speculum examination, which was managed expectantly, except in cases where there was a suspicion of malignancy. None of the study subjects with cervical polyps had abnormal cervical smears during pregnancy. They sought to examine if cervical polyps had an impact on spontaneous preterm birth before 34 weeks of gestation. Women with fetal anomalies, multiple pregnancies, loss of pregnancy before 12 weeks of gestation were not included in the trial.

Out of the 4,172 selected participants, 92 (2.2%) were found to have a cervical polyp before 12 weeks of gestation. But polypectomy was not performed. Pregnant women who had cervical polyps were 4 times more likely to have spontaneous preterm births before 34 weeks of gestation compared to women who did not have cervical polyps; 5.4% vs. 0.7%, respectively with adjusted odds ratio (OR) of 4.09. After adjusting for confounding variables such as smoking, underweight prior to conceiving, the adjusted hazard ratio (aHR) for spontaneous preterm birth before 34 weeks of gestation among women with polyps compared to those without cervical polyps was 2.95.

Based on these findings, the authors suggest that unremoved cervical polyps diagnosed in early pregnancy are a risk factor for spontaneous preterm birth before 34 weeks of gestation. Clinicians should be aware of the association between cervical polyps and spontaneous preterm birth and encourage their patients to adopt healthy lifestyle habits.

Reference

1. Wakimoto T, et al. Relationship between unremoved cervical polyp in pregnancy and spontaneous preterm birth. Am J Obstet Gynecol. 2022;227(6):899.e1-899.e6.

Atopic Dermatitis and Risk of Fracture

Children with atopic dermatitis (AD) are at higher risk of suffering a fracture, suggests a recent study from South Korea published in the journal *Allergy*.[1] The risk increased proportionately with the severity of the disease.

To examine the association between AD and incidence of fractures, data of 1,778,588 children born between

2009 and 2015 was scrutinized. Information was sourced from the first National Health Screening Program for Infants and Children and evaluated for location of fracture and time of fracture. The follow-up period was an average of 7.52 years.

A total of 3,42,601 children (19.3%) examined were diagnosed with AD. Children with AD were 14% more likely to develop fractures (33.37 vs. 28.88 per 1,000 person-years, respectively). The risk of fracture increased as the severity of AD increased; children with moderate to severe AD were at the highest fracture risk (35.54 per 1,000 person-years) compared to children with mild AD (33.08 per 1,000 person-years) and children in the control group (28.88 per 1,000 person-years).

Children with mild AD were at 12% higher risk of fracture with aHR of 1.12, while the fracture risk increased by 23% among patients with moderate to severe AD (aHR 1.23).

Age at diagnosis was found to affect the risk of fracture. In children younger than 2 years, the aHR for fracture risk was 1.19, for children aged 2 to 4 years, the aHR was 1.08, while in children aged ≥5 years, the aHR was 1.03. The risk was maximum in the first year after the diagnosis of AD with aHR of 1.53, although the risk continued for up to 5 years (aHR 1.35). The effect was similar for the different fracture sites assessed: head (aHR 1.13), spine (aHR 1.33), upper limb (aHR 1.06), lower limb (aHR 1.13) and other sites (aHR 1.21). The enhanced risk of fractures is multifactorial, state the authors and may include dietary habits, intake of calcium and vitamin D, physical activity, sleep quality and effect of systemic corticosteroids.

This study shows that children with AD were at a higher risk of fracture. The risk was highest among children diagnosed at an early age. Most fractures occurred within the first year of diagnosis.

Reference

1. Lee SW, et al. Fracture incidence in children after developing atopic dermatitis: A Korean nationwide birth cohort study. Allergy. 2022 Nov 9. [Epub ahead of print]

Study Implicates Five Bacteria in Global Infection-related Mortality

Five pathogens – *Staphylococcus aureus*, *Escherichia coli*, *Streptococcus pneumoniae*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* accounted for the majority of global deaths due to infectious diseases in 2019. In this first-time audit of deaths published in *The Lancet*, bacterial infections were found to be the second most important cause of death after ischemic heart disease.[1]

In this study, researchers assessed the infection-related deaths that occurred in 2019 in 204 countries in 11 infectious diseases caused by 33 clinically significant bacterial species. Data for this analysis was obtained from the Global Burden of Diseases, Injuries and Risk Factors Study (GBD) 2019 and the Global Burden of Antimicrobial Resistance 2019 study. *Mycobacterium tuberculosis* was not included in this analysis because there is already an End TB strategy in places globally with many countries having dedicated TB control programs. The researchers estimated the number of infection-related deaths, the infectious disease implicated in the deaths and the pathogens causing the infectious disease. Aided by these three modeling steps, number of deaths associated with each pathogen was estimated.

A total of 14 million infection-related deaths were recorded in 2019. Of these, nearly 8 million deaths were associated with the 33 species of bacteria examined. Amongst all the bacterial species evaluated, five bacteria namely *S. aureus, E. coli, S. pneumoniae, K. pneumoniae* and *P. aeruginosa* accounted for nearly 55% of deaths. *S. aureus* was associated with more than 1 million deaths globally in 2019, while more than 5,00,000 deaths each could be attributed to the remaining four pathogens.

Lower respiratory infections (4 million), bloodstream infections (2.91 million) and peritoneal and intra-abdominal infections (1.28 million) accounted for the majority of deaths in 2019. *S. aureus* was associated with 6,53,000 deaths due to lower respiratory tract infections (LRTIs) and 2,99,000 deaths due to bloodstream infections, while *E. coli* was linked to 2,90,000 deaths due to peritoneal and intra-abdominal infections. A regional difference was noted with highest mortality burden reported in sub-Saharan Africa (230 deaths per 1,00,000 population) vis-à-vis 52.2 deaths per 1,00,000 population in the high-income regions. The major pathogen responsible for deaths in persons aged ≥15 years was *S. aureus*, while among children ≤5 years, the major organism causing death was *S. pneumoniae*.

This study, which was conducted in the pre-COVID era, has identified 5 pathogens that were implicated in majority of deaths that occurred in 2019 due to infectious causes. As the "second leading cause" of death globally in 2019, an urgent action and intervention is necessary starting with increased and better surveillance. Prevention of infection, rational use of antibiotics, improved microbiological testing and vaccination are few approaches to tackle this high burden of bacterial infections and prevent mortality.

Reference

1. GBD 2019 Antimicrobial Resistance Collaborators. Global mortality associated with 33 bacterial pathogens in 2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2022;400(10369):2221-48.

CLEAR Outcomes Clears the Way for Bempedoic Acid as the First Nonstatin Lipid-lowering Treatment Option

Top line results of the CLEAR Outcomes trial have been published and they bring great cheer for patients with statin intolerance at high risk for adverse cardiovascular (CV) events. The trial met the primary composite endpoint of CV death, nonfatal myocardial infarction (MI), nonfatal stroke and unstable angina requiring hospitalization by demonstrating a significant decrease in major cardiovascular events (MACE) in patients treated with bempedoic acid compared to placebo. This makes bempedoic acid the first nonstatin drug in the class of ATP-citrate lyase inhibitors, to demonstrate significant and "clinically meaningful" effects in the treatment of statin intolerant patients, according to a press release from the manufacturer Esperion.[1,2]

At this point of time, however, we do not have enough details about the results. Only the top line results have been released. The complete data is likely to be shared in the coming year.

About the CLEAR Outcomes trial

The **C**holesterol **L**owering via b**E**mpedoic **A**cid, an ACL-Inhibiting **R**egimen (CLEAR) Outcomes trial, conducted in 32 countries, examined the effects of 180 mg daily bempedoic acid in lowering the elevated lipid levels (low-density lipoprotein cholesterol [LDL-C] ≥100 mg/dL) and its ability to reduce the occurrence of MACE in at-risk patients in whom statins and other lipid-lowering drugs failed to reach the optimal lipid targets. The randomized, double-blind, placebo-controlled trial had enrolled nearly 15,000 patients with cardiovascular disease (CVD) or those who are at high risk for CVD and had exhibited intolerance to at least 2 statins.

Bempedoic acid was Food and Drug Administration (FDA) approved in February 2020 as an adjunct to diet and maximally tolerated statin therapy for the treatment of adults with heterozygous familial hypercholesterolemia or established atherosclerotic cardiovascular disease (ASCVD) who require additional lowering of LDL-C in the dose of 180 mg administered orally once daily.

However, the press release has cautioned about the simultaneous use of bempedoic acid with simvastatin or pravastatin due to the risk of risk for "simvastatin- or pravastatin-related myopathy."

References

1. https://www.esperion.com/news-releases/news-release-details/esperion-announces-clear-cardiovascular-outcomes-trial-nexletolr. December 7, 2022.
2. Bempedoic acid cuts CV risk in the statin-intolerant: CLEAR top-line results – Medscape. Dec 07, 2022.

Rheumatoid Arthritis Medicine Found Helpful in Reducing Risk of Heart Disease

A recent study published in the *Annals of Rheumatic Diseases* found that treatments often given to patients to lower joint inflammation may also reduce the risk of CVD in those with rheumatoid arthritis (RA), who are at an increased risk for the condition. Patients with moderate to severe RA are typically treated with methotrexate as their first-line of defense, although most RA patients eventually transition to tumor necrosis factor inhibitor (TNFi) or triple therapy (methotrexate plus sulfasalazine and hydroxychloroquine). In the current study, 115 persons with moderate to severe RA were given a TNFi, either adalimumab or etanercept, despite receiving methotrexate. The other option was triple therapy. Both groups experienced comparable declines in arterial inflammation, a risk factor for heart disease and RA disease activity after 6 months. Experts were overwhelmed to observe that these potent anti-inflammatory medications decreased the risk of heart disease in RA patients. They emphasized that the typical risk factors for heart disease, such as high cholesterol, high blood pressure and obesity, still need to be considered by doctors. But since inflammation—a crucial aspect of RA—increases the CV risk even more; treating arthritis offers a novel way to lower these people's risk of heart disease. (*Source: https://theprint.in/health/study-risk-of-heart-disease-can-be-reduced-by-rheumatoid-arthritis-medicine/1258774/*)

First Center of Excellence for 3D Bioprinting Inaugurated by IISc

The first 3D bioprinting Center of Excellence (CoE) in the nation was opened on 9th December, following an agreement reached in August between CELLINK, a pioneer in bioprinter development, and the Indian Institute of Science (IISc). It will concentrate on giving scientists the resources they need to enhance research in drug development, tissue engineering and regenerative medicine. According to a news release from IISc, the CoE, which will be based in the Institute's Centre for BioSystems Science and Engineering (BSSE), will give researchers access to 3D bioprinting equipment,

allowing them to move more quickly toward the ultimate objective of enhancing health outcomes.

Tomoko Bylund, head of sales at CELLINK, said that the center offers cutting-edge, market-leading 3D bioprinting technology. These technologies will make substantial advances in research and the development of the future of health care. Researchers will have access to CELLINK instruments located at the center, such as the "BIO X, BIO X6 and the BIONOVA X". (*Source: https://health.economictimes.indiatimes.com/news/industry/iisc-inaugurates-first-centre-of-excellence-for-3d-bioprinting/96128840*)

Study Reveals Gene behind Our Smoking and Drinking Behaviors

A recent study suggests that smoking and drinking habits may also be influenced by our genes, even though these behaviors are primarily controlled by many environmental and social factors. More than 3,500 genetic variants have been linked in studies to potential effects on this behavior. Given that these behaviors can put health at danger from psychiatric and CV problems and those hereditary factors might affect these behaviors, there is now much that can be done to try to change these behaviors. The study has concentrated chiefly on people in Europe. The scientists created a model for the study using the genetic information of 3,383,199 individuals, 21% of whom were of non-European origin. There are currently 3,823 genetic variations known to affect drinking or smoking habits. A total of 243 genes are associated to how many cigarettes a person will smoke in a day, and 849 genetic variants are linked to how many alcoholic beverages a person will consume each week. Thirty-nine genes are linked to the age at which someone will start smoking. Researchers found that most genetic correlations between smoking and drinking had similar consequences. They further stated that the environmental and epigenetic variables play critical role in turning the genes on and off, hence differences are less. (*Source: https://www.livemint.com/science/health/gene-determines-our-smoking-and-drinking-habits-here-s-what-study-shows-11670601360514.html*)

Strong Association Found Between High Levels of Arsenic Contamination in Water and Antibiotic Resistance Carriage among Children

A recent study published in *PLOS Pathogens* found that rural Bangladesh, which has high levels of arsenic poisoning in drinking water, had a greater prevalence of antibiotic-resistant *E coli* in both water and child stool samples. Antibiotic resistance is one of the primary causes of hospital admissions and fatalities worldwide. Researchers in the current study analyzed water and stool samples from 100 families in two rural Bangladeshi subdistricts, including mothers and young children. Overall, *E. coli* was detected in 84% of water and stool samples from the Hajiganj and Matlab locations. Antibiotic-resistant was substantially more prevalent among children in Hajiganj (94%) than in Matlab (76%), and in water in Hajiganj (48%) compared to water in Matlab (22%, $p < 0.05$), but not among mothers. Additionally, a larger percentage of *E. coli* infections from Hajiganj were not effectively treated due to resistance to multiple antibiotics such as penicillin, cephalosporin and chloramphenicol. Experts further stated that heavy metals like arsenic that result in antibiotic resistance in children are a significant public health problem and need immediate measures to decrease arsenic exposure. (*Source: https://www.news-medical.net/news/20221208/High-levels-of-arsenic-contamination-in-water-linked-to-antibiotic-resistance-carriage-among-children.aspx*)

Vaginal Estrogen and Use of Pessaries

Vaginal pessaries are a noninvasive therapeutic option in the management of pelvic organ prolapse. Vaginal pessaries are, however, a stopgap measure, until surgery is performed. While they provide symptomatic relief, their use is often associated with adverse effects such as increased vaginal discharge. A systematic review and meta-analysis of 5 RCTs and cohort studies published in the journal *Climacteric* has examined the effect of using local estrogen along with a vaginal pessary on adverse effects in postmenopausal women with pelvic organ prolapse.[1] Analysis revealed that women who used estrogen together with vaginal pessary showed a marked lower incidence of bacterial vaginosis compared to controls with OR of 0.29. The OR for vaginal ulceration was 0.98, for vaginal bleeding it was 0.80 and for vaginal discharge it was 0.74. This study has demonstrated the beneficial effect of the use of local estrogen together with a vaginal pessary in reducing the rate of bacterial vaginosis among postmenopausal women with pelvic organ prolapse. At the same time, the authors note the lack of consensus regarding the concurrent use of estrogen for lessening the other complications of pessaries and advocate larger studies to analyze the effect of estrogen use on reducing pessary-related complications.

Reference

1. Ai F, et al. Effect of estrogen on vaginal complications of pessary use: a systematic review and meta-analysis. Climacteric. 2022;25(6):533-42.

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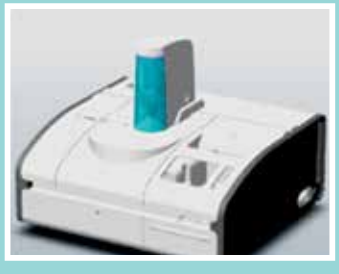

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Why Do We Put on Tilak on the Forehead?

The Tilak is a mark of auspiciousness and invokes a feeling of respect in the wearer and others. It is recognized as a religious mark. Its form and color vary according to one's caste, religious sect or the form of worship of the person in question. Tilak is applied on the forehead with sandal paste, sacred ash or kumkum, a red turmeric powder. In a wedding, a Kumkum tilak is applied on the forehead of both the bride and groom.

In earlier times, the four castes (based on varna or color) – Brahmana, Kshatriya, Vaishya and Shudra – applied marks differently. The Brahmin applied a white chandan mark signifying purity, as his profession was of a priestly or academic nature. The Kshatriya applied a red kumkum mark signifying valor as he belonged to the warrior race. The Vaishya wore a yellow kesar or turmeric mark signifying prosperity as he was a businessman or trader devoted to creation of wealth. The Shudra applied a black bhasma, kasturi or charcoal mark signifying service as he supported the work of the other three castes.

The devotees of Shiva apply sacred ash (Bhasma) on the forehead as a Tripundra (three parallel horizontal lines); the devotees of Vishnu apply sandal paste (Chandan) in the shape of "U" and the worshippers of Devi or Shakti apply Kumkum.

The Tilak is applied in the spot between the eyebrows, which is the seat of memory and thought. It is known as the Aajna Chakra in the language of Yoga. The Tilak is applied with the prayer – "May I remember the Lord. May this pious feeling pervade all my activities. May I be righteous in my deeds?" Even when we temporarily forget this prayerful attitude, the mark on another reminds us of our resolve. The Tilak is thus a blessing of the Lord and a protection against wrong tendencies and forces. The entire body emanates energy in the form of electromagnetic waves – the forehead and the spot between the eyebrows especially so. That is why worry generates heat and causes a headache. The Tilak cools the forehead, protects the wearer and prevents energy loss. Sometimes, the entire forehead is covered with chandan or bhasma.

Using plastic reusable "stick bindis" is not very beneficial, even though it serves the purpose of decoration.

■■■■

Atopic Dermatitis: A Risk Factor for Incident Migraine?

The likelihood of occurrence of new-onset migraine is high in patients with atopic dermatitis (AD), suggests a study of nearly 50,000 AD published in the *Journal of the European Academy of Dermatology & Venereology*.[1,2]

A team of researchers from South Korea screened 3.5 million adults, who had a health check-up done in 2009, from the Korean National Health Insurance Service claims database. Out of these, 48,983 adults (1.5%) were found to be diagnosed with AD. Over the median follow-up period of 7.6 years, 449,484 new-onset migraine cases were identified. The cumulative incidence of new-onset migraine was 21.8 per 1,000 person-years among patients with AD, whereas in patients without AD, the incidence of incident migraine was 16.5 per 1,000 person-years with hazard ratio (HR) of 1.26. Patients with moderate to severe AD were at higher risk of suffering new-onset migraine than patients with mild form of the disease (HR 1.26). Being male and a smoker further added to the risk. Similarly, AD patients with sleep disorders or stroke were also at risk of incident migraine. This study has shown an association of AD with new-development of migraine and has also identified factors associated with elevated risk. However, the authors state, "Further study is needed to examine whether appropriate management of AD can guard against the risk of new-onset migraine."[2]

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INSPIRATIONAL STORY

Emotional Management

When someone is doing something or is about to do something, in a way we don't want it to be done and when we are not able to accept it, we become angry.

However, when someone is doing something or is about to do something, in a way we don't want it to be done – and we are able to accept it – we remain tolerant.

When someone has something which we don't have, or someone is able to produce the results which we are not able to produce – and we are not able to accept it – we become jealous.

When someone has something which we don't have, or someone is able to produce the results which we are not able to produce and we are able to accept it – we get inspired.

Then emotional equation is quite simple.

Something + Acceptance = Positive Emotion

Something + Nonacceptance = Negative Emotion

So, it is not 'something' or 'someone' who is making us feel positive or negative, but it is our 'acceptance' or 'nonacceptance' of something or someone, which is making us feel positive or negative.

It isn't the world but the quality of our response to the world that determines the quality of our emotions. Next time, we feel disturbed with a negative emotion, instead of asking who or what is disturbing us, we will examine who or what we are resisting (not accepting) that is causing this disturbance in us. We will replace resistance (nonacceptance) with acceptance, and the negative emotion will turn into a positive one.

Emotional management begins by stopping to blame that 'something' or 'someone' and starting to take the responsibility to respond life with 'acceptance'.

■■■■

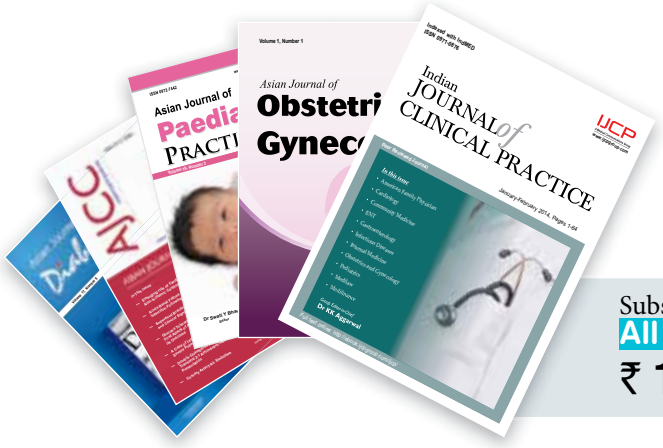
Hidden Tobacco Marketing on Social Media Uncovered in a Report

Approximately 29% of the adult (15+) population still uses tobacco, despite the reduction in tobacco use across the country. In India, there are strong policies restricting tobacco advertising, promotion and sponsorship, yet "surrogate marketing" is being used on traditional media channels to indirectly promote unregulated tobacco products, such as pan masala, etc.

A report released recently, titled "Hidden in Plain Sight: Surrogate Marketing of Tobacco Products on Social Media in India," offered a look at surrogate marketing on social media platforms. The report captured and analyzed more than 2,000 posts collected between January and May 2022 that indirectly promote tobacco. It was seen that 12% of the posts promoted tobacco through surrogate marketing.

The key findings of the reports were that out of 2,111 instances of online tobacco marketing, more than 90% were for tobacco companies' allied products, including surrogate products and brand-extended products. These findings also highlighted 243 instances of online surrogate marketing (12%), 1,691 instances of company brand extension marketing (80%) and 8% of other instances that were directly marketing tobacco products. The report also revealed that three-fourths (75%) of the online surrogate marketing was observed on meta platforms (Facebook and Instagram).

Additionally, it was also observed that these surrogate marketing ideas leveraged cultural festivities and featured celebrities. All surrogate marketing promoted mouth fresheners and pan masala products as smokeless tobacco products (100%) while, in 98% of the cases, the product included a clear product picture and the tobacco company's logo. (*Source: https://health.economictimes.indiatimes.com/news/industry/new-report-uncovers-hidden-tobacco-marketing-on-social-media/96265622*)



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Lighter Side of Medicine

HUMOR

TOP SECRET COMMUNICATIONS CENTER

When my son was in the Air Force, my wife and I visited quite often. On our first visit, we were allowed inside this top secret Communications Center, but everything in sight was covered up so we could look around everywhere — Heck, even the toilet paper in the Men's room was disguised.

Anyway, at the exit, there's a sign above the door, which reads: "You have been exposed to Top Secret Material. Please destroy yourself before leaving the building." Matka was caught by the police.

Police: How did you kill 20 people..?

Matka: Mai gaadi tez chala raha tha par jab maine brake lagaya, to pata laga ki brake fail ho gaye hai. Phir maine saamne dekha to 2 aadmi ja rahe the… doosri taraf 1 barat ja rahi thi. Ab aap batao mai gaadi kidhar modta..?

Police: Of course, jis taraf 2 aadmi the. Nuksan kam hota.

Matka: Exactly. Maine bhi yehi socha tha par woh 2 aadmi meri gaadi dekh kar barat me ghus gaye… Toh mai kya karta!!!

FAINTING

The man passed out in a dead faint as he came out of his front door onto the porch. Someone called 911.

When the paramedics arrived, they helped him regain consciousness and asked if he knew what caused him to faint.

"It was enough to make anybody faint," he said. "My son asked me for the keys to the garage, and instead of driving the car out, he came out with the lawn mower!"

STUDENT WHO OBTAINED 0% ON AN EXAM

Q. In which battle did Napoleon die?

A. His last battle

Q. Where was the Declaration of Independence signed?

A. At the bottom of the page.

Q. River Ravi flows in which state?

A. Liquid

Q. What is the main reason for divorce?

A. Marriage

Q. What is the main reason for failure?

A. Exams

Q. How can a man go 8 days without sleeping?

A. No problem, he sleeps at night.

Q. How can you lift an elephant with one hand?

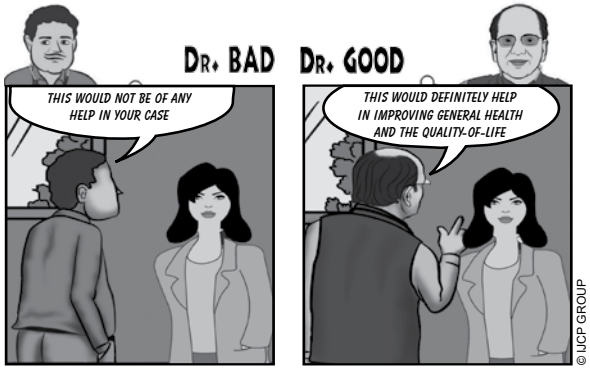
A. You will never find an elephant that has only one hand.

Q: How can you drop a raw egg onto a concrete floor without cracking it?

A. Any way you want, concrete floors are very hard to crack.

Dr. Good and Dr. Bad

SITUATION: A 30-year-old female with a history of GDM was planning second pregnancy. She was advised to indulge in leisure-time physical activity and maintain cardiorespiratory fitness.



LESSON: A positive relationship of cardiorespiratory fitness and leisure-time physical activity has been demonstrated with perceived general health and physical well-being in females planning pregnancy and are at risk for GDM. Thus, even a slightly better cardiorespiratory fitness in those with low levels would prove to be beneficial.

Scand J Med Sci Sports. 2018;28:203-11.

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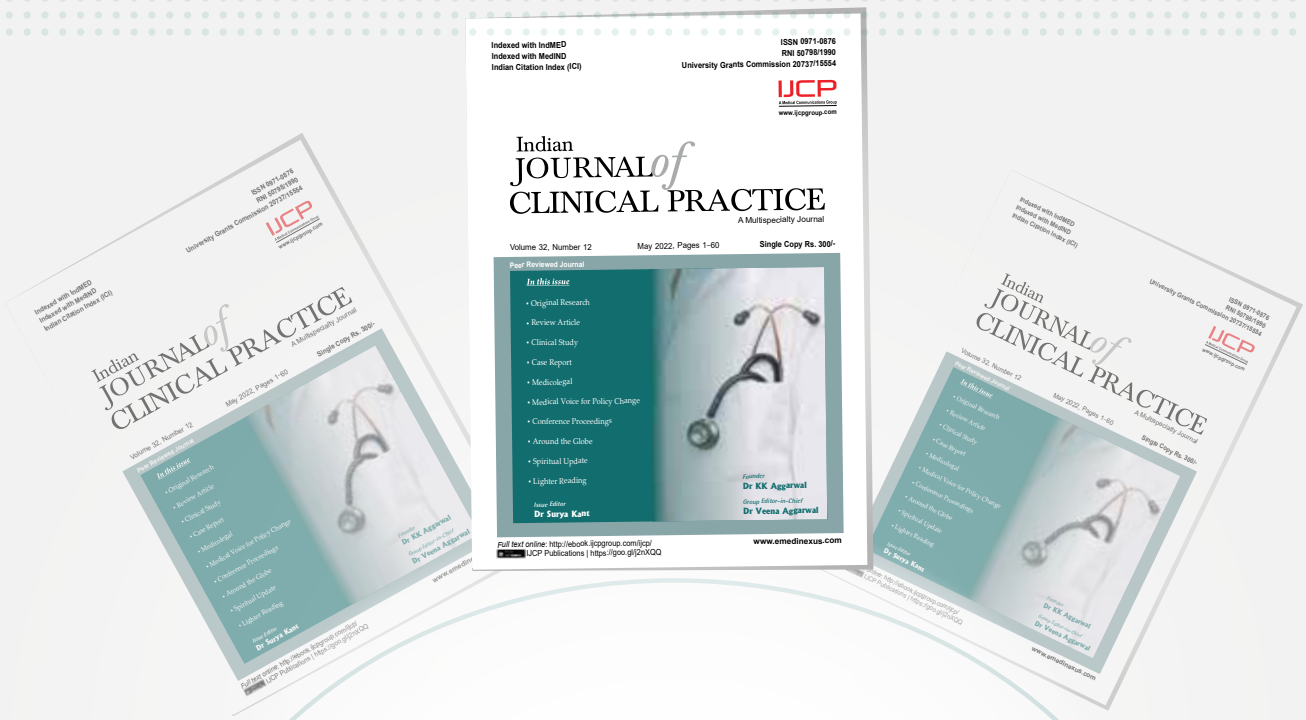

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Paintal AS. Impulses in vagal afferent fibres from specific pulmonary deflation receptors. The response of those receptors to phenylguanide, potato S-hydroxytryptamine and their role in respiratory and cardiovascular reflexes. Q. J. Expt. Physiol. 1955;40:89-111.

Books

Stansfield AG. Lymph Node Biopsy Interpretation Churchill Livingstone, New York 1985.

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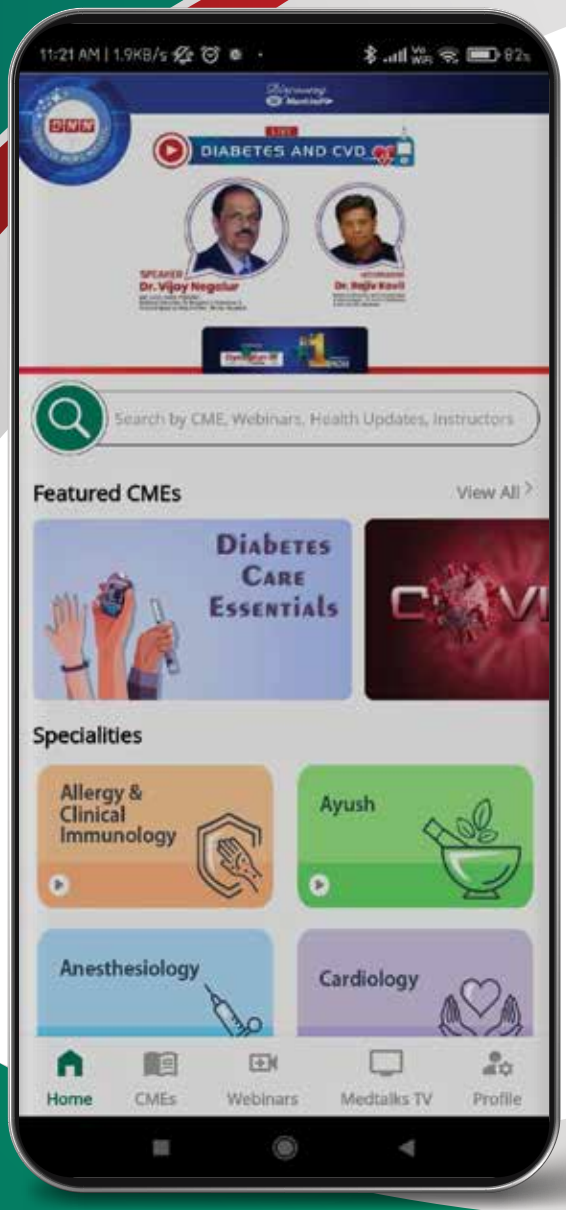

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