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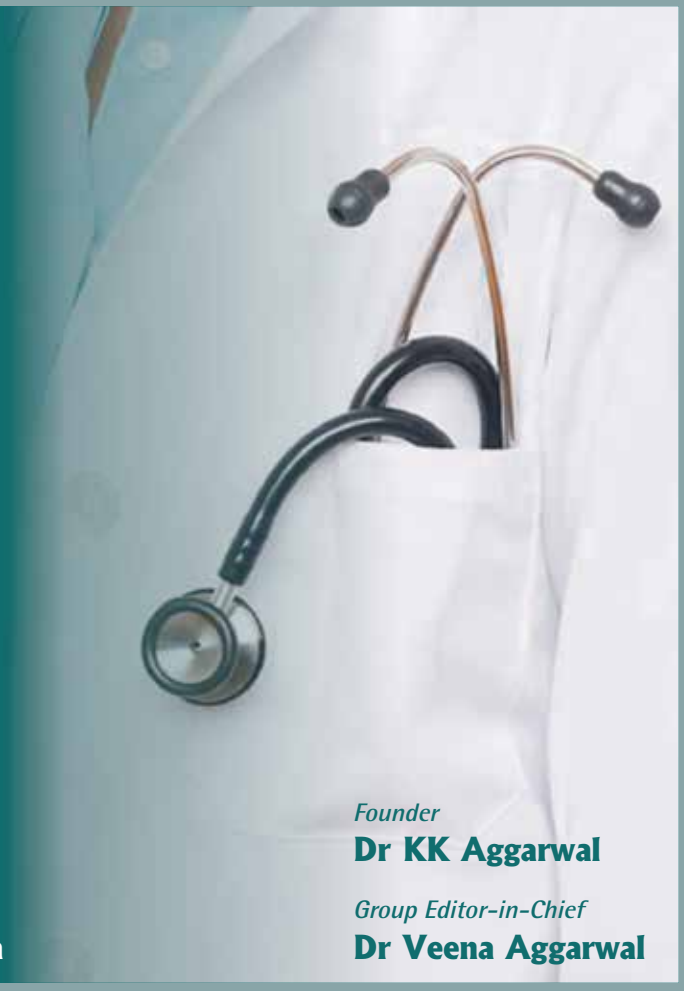

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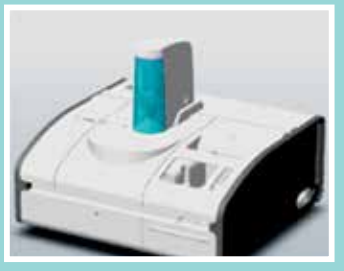

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Risk Factors for Postmenopause Depressive Symptoms

Women with depressive symptoms preceding the final menstrual period (FMP) are at greater risk of developing depression during the postmenopause, according to results from the Study of Women's Health Across the Nation (SWAN) recently published in the journal *Menopause*.[1]

A total of 1,551 middle-aged participants from the Study of Women's Health Across the Nation were included in the present study. A longitudinal analysis of the data on depressive symptoms gathered from 1996 to 2017 among the selected women was longitudinally analyzed over 19 years (median) to examine depressive symptoms during postmenopause and the contribution of depressive symptom trajectories before the FMP. The study also examined the impact of psychosocial/health factors on the postmenopause depressive symptoms.

Compared to premenopause stage, the probability of depressive symptom scores of 16 or higher on the Center for Epidemiologic Studies Depression Scale (CES-D) was greater during postmenopause with odds ratio (OR) of 1.49, but not during the menopausal transition or perimenopause. Based on the scores, three pre-FMP groups were defined: Group 1 (47.7%), consistently low scores, Group 2 (39.9%), moderate scores below the high depressive symptom threshold and Group 3 (12.4%), consistently high scores.[1] Women with moderate scores on the depression scale were nearly threefold more likely to have higher scores when postmenopausal with OR of 2.62, whereas women who scored high on the depression scale were at nearly sevenfold greater risk of higher scores during the postmenopause with OR of 6.88.

History of severe anxiety, sleep problems, vasomotor symptoms, low social support and childhood trauma/maltreatment before reaching the FMP were also identified as contributing to higher odds of depressive symptoms during postmenopause.

World Menopause Day is held every year on 18th October and the theme for this year is "Cognition and Mood". Hot flashes and night sweats are typically associated with menopause. However, the symptoms of menopause are wide-ranging. They include mood problems among several others. Earlier studies have shown that mood problems may adversely affect cognition. Hence, women approaching menopause should be regularly screened for risk factors predisposing to depressive symptoms later on and provided with appropriate treatment for a better quality of life.

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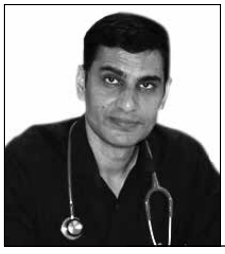

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Insulin is Essential: The National List of Essential Medicines, India, 2022

Insulin is essential for life. While most persons produce adequate amounts of insulin, not everyone is lucky enough. Persons living with type 1 diabetes, with pancreatic diabetes, and with severe or long-standing type 2 diabetes need exogenous insulin for survival.[1] Many persons with type 2 diabetes and comorbidities such as renal or hepatic impairment, severe sepsis or infection, also require insulin. It is the drug of choice for glycemic control during pregnancy. Unfortunately, insulin is expensive, and may be out of reach for many people who need it.[2] One way of ensuring affordable insulin is to declare it an essential drug.

INDIA'S NATIONAL LIST OF ESSENTIAL MEDICINES

The National List of Essential Medicines (NLEM), India reflects this thought process. Successive editions of the NLEM have included various preparations and strengths of insulin.[3,4] This year, the NLEM lists four insulins: soluble, NPH (neutral protamine Hagedorn), premixed insulin and glargine, irrespective of delivery device.[5] It is assumed that all strengths (40 IU/mL and 100 IU/mL for human insulin, and 100 U/mL for glargine) are included in the essential list. The 50:50 premixed insulin preparation is not included in NLEM, though it must be admitted that it is not as commonly prescribed as the 30:70 preparation.

The addition of insulin glargine in the Indian NLEM is a welcome development. This underscores the acceptance of the need to provide safe and effective medication to persons living with diabetes at an affordable cost. The updated NLEM highlights India's commitment towards providing world-class treatment to its citizens, and ensuring that the noncommunication disease epidemic is addressed aggressively. The Indian pharmaceutical industry has contributed immensely to the production of economical and efficient insulin, not only for the domestic, but also for the global market.[6] An Indian insulin glargine brand has received a label for interchangeability with originator brands from the United States Food and Drug Administration (US FDA).[7]

This implies the quality and robustness in clinical data and more importantly "a Make in India product to meet the global need" which addresses two key barriers, i.e., affordability and accessibility of insulin for all. US FDA defines Interchangeable if the biological product "is biosimilar to the reference product" and "can be expected to produce the same clinical result as the reference product in any given patient."[8] The 'interchangeable' status can prompt faster and wider uptake of insulin biosimilars and keep the insulin expenditure under control, especially for patients who otherwise practice nonadherence or rationing of life-saving insulin.

NATIONAL LISTS OF ESSENTIAL DEVICES AND ESSENTIAL DIAGNOSTICS

Persons living with diabetes need much more, though. Just as insulin preparations are essential, so are the insulin delivery devices like syringes, pens and pumps.[9] Insulin monitoring systems, such as glucose monitors, urine sugar strips, ambulatory/continuous glucose monitoring systems are equally essential to ensure safe and accurate therapy. Equal emphasis should therefore be placed on diabetes care in the National Lists of Essential Devices and Essential Diagnostics.

NONINSULIN MEDICATIONS

The 2022 NLEM contains a brief, yet comprehensive, list of noninsulin oral medications.[5] Their listing reflects the increasing disease burden of diabetes, as well as the efficacy, safety and cost-effectiveness of the drug. Teneligliptin, a dipeptidyl peptidase 4 (DPP-4) inhibitor has been added this year. The sulfonylurea glimepiride, and the insulin sensitizer, metformin, complete the list. No sodium-glucose co-transporter 2 (SGLT2) inhibitor or glucagon-like peptide 1 receptor agonists (GLP-1RA) figure in the list, however.

SUMMARY

As we work towards becoming the Diabetes Care Capital of the world (Prof BK Sahay, personal communication), each and every stakeholder's involvement is important. Diabetes care cannot be achieved without ensuring availability, accessibility and affordability of diabetes related diagnostics, drugs and devices. The NLEM 2022 demonstrates the commitment of the Indian government towards achieving this goal. Sustained and concerted efforts will be needed in the future as well, to accomplish our goals.

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■■■■

Medication-associated Changes in Hair Texture

Hair texture may alter as a side effect of medications, according to a study published in the *Journal of Drugs in Dermatology*.[1] Hair texture changes were most commonly associated with antineoplastic drugs.

Researchers carried out a review of 31 published articles involving 2,594 patients to characterize the changes in hair texture associated with medications and to also find out the most commonly implicated drugs. The articles were searched from PubMed and Cochrane databases. The average age of the study subjects was 48.4 years and about 42% of them were female.

Analysis of data revealed antineoplastic drugs (n = 97) were most commonly associated with hair texture changes. The antiepileptics (n = 56) were the second most common group. The other drug classes associated with hair texture changes were retinoids (n = 15), immunomodulators (n = 3) and antiretrovirals (n = 1).

The most common types of textural changes were *de novo* or exaggerated curling patterns, i.e., curling of straight hair or more curling of curly hair. Kinking, waving of hair were also seen. The changes occurred within 5 months following use of immunomodulator drugs, whereas with antiretrovirals, the hair texture changes took 17 months to appear. While most changes reversed in 3 week to 5 years after the therapy, the changes associated with the use of antiretrovirals, retinoids and antineoplastics were irreversible.

This study has correlated hair texture changes with five groups of drugs: antineoplastics, antiepileptics, retinoids, immunomodulators and antiretroviral therapy. Side-effects are undesired effects of medications and any change in the texture of hair may have psychosocial impact on the patient. Hence, clinicians should be aware of this potential side effect and communicate to the patient before initiating treatment with these drugs.

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REVIEW ARTICLE

Will Oral Semaglutide be a Game-Changer in the Management of Type 2 Diabetes in Indian Context?

ARJUN BAIDYA*, SAURABH MISHRA†, ASHOK VENKATANARASU‡

ABSTRACT

The glucagon-like peptide-1 receptor agonists (GLP-1RAs) have important beneficial effects on glycemic control and body weight along with their pleiotropic effects on various systems of the body. However, until now these agents were administered via an injection posing a challenge to patient convenience. Oral semaglutide is a first in class oral GLP-1RA co-formulated with an absorption enhancer for the treatment of type 2 diabetes mellitus (T2DM). The clinical efficacy and safety of oral semaglutide has been extensively evaluated in the Peptide InnOvatioN for Early diabEtes tReatment (PIONEER) program of clinical trials. This review shall elaborate on the unique diabetes situation in India and why the oral GLP-1RA (semaglutide) will be a game-changer in the Indian setting.

Keywords: Semaglutide, type 2 diabetes, GLP-1RAs, glucose-lowering drugs

Type 2 diabetes mellitus (T2DM) accounts for almost 90% of all diabetes cases worldwide. The prevalence of diabetes around the world will reach up to 592 million by the year 2035.[1] The genetic component among South Asians makes them up to four times more susceptible to T2DM compared to other ethnic groups.[2] The concept of an "Asian Indian Phenotype" was advanced by Mohan et al,[3] as the presence of insulin resistance along with abdominal obesity, higher C-reactive protein (CRP) and lower levels of adiponectin. Asian Indians have a lean-fat body composition with higher levels of central obesity (waist circumference, waist-to-hip ratio and visceral fat). They also have more body fat for a given body mass index (BMI) compared to other ethnic groups.[4] Thus, the lean-fat Indian is at a larger risk of diabetes, which results from genetic predisposition along with other factors like lifestyle changes, rapid urbanization and changing dietary patterns.

The baseline data of Indian type 2 diabetic patients in an observational study showed high prevalence of micro- and macrovascular complications due to poor glycemic control (mean glycated hemoglobin [HbA1c] = 9.2 ± 1.4).[5] The relation between glycemic status and incidence of complications highlights the importance of optimum glycemic control in T2DM. The glycemic control, however, continues to deteriorate as the disease progresses.[6]

Obesity which is often described as 'Diabesity' in obese type 2 diabetics is a major risk factor leading to hypertension, hyperlipidemia, atherosclerotic cardiovascular disease (ASCVD) and its complications, and also to many types of cancers.[7] The prevalence of diabesity is reaching epidemic proportions around the globe with no clear guidelines for its optimum management.[8] In Indian adults aged 20 to 69 years, the prevalence of overweight will more than double while the prevalence of obesity will triple by 2040.[9]

The management of patients with T2DM has become individualized with different therapies available and presence of specific patient factors that influence the appropriate choice of medication. In 2018, the American Diabetes Association (ADA) presented a decision algorithm, which included assessment of key

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patient characteristics including comorbidities like ASCVD, chronic kidney disease (CKD) or heart failure (HF). The presence of these comorbidities should allow preferential use of certain classes of glucose-lowering drugs as second-line therapy.[10]

Glucagon-like peptide-1 receptor agonists (GLP-1RAs) are an established class of glucose-lowering drugs, which have a pleiotropic action on the pathophysiological defects of T2D, leading to effective glycemic control, loss of weight, minimal risk of hypoglycemia and a consistent safety profile.[11]

GLP-1RAs have similar mechanism of action but they vary in structure, pharmacokinetics and efficacy (their ability to reduce HbA1c, body weight and cardiorenal protection).[12,13]

The previous success in clinical trials of exenatide and liraglutide renewed interest in the GLP-1 therapy area. The daily injection regime was inconvenient for some patients and so better patient convenience was needed for patient adherence and satisfaction.[14] The fear of injections and difficulty in administration along with the perception of injectable therapy was a major barrier to the use of GLP-1RA therapy.[11]

Semaglutide is a GLP-1RA with 94% structural homology to endogenous GLP-1, and it has three important structural differences that prolong its half-life but do not compromise receptor binding. The efficacy and safety of subcutaneous semaglutide is already demonstrated in numerous clinical studies. The efficacy of oral semaglutide was expected to correspond with subcutaneous semaglutide and was proved with the Peptide InnOvatioN for Early diabEtes tReatment (PIONEER) studies.[15]

Oral semaglutide is co-formulated with SNAC {Sodium N-[8-(2-hydroxybenzoyl)amino]caprylate} which is an absorption enhancer and promotes semaglutide absorption across the gastric mucosa. This review will specifically elaborate on why oral semaglutide will be ideal for Indian diabetic patient in the light of evidence from studies on oral and injectable semaglutide.

DIABETES AND PREDIABETES

The Indian Council of Medical Research-India Diabetes (ICMR-INDIAB) study was a national study designed to estimate the prevalence of diabetes and prediabetes in Indian population. It was the largest ever study conducted to capture the diabetes picture in India.

The prevalence findings were reported from 15 states, which represented 50.7% of the adult population of the country. The main factors identified to be driving the epidemic of diabetes in India were obesity, age and a family history of T2DM. Prediabetes prevalence in India was high and exceeded diabetes in many states implying a huge risk of progression to overt diabetes.[16] This finding is very important in the Indian context as it has been shown in several studies that Asian Indians progress faster through the prediabetes stage when compared with other ethnic groups.[17]

Beta-cell dysfunction was prominent even with mild dysglycemia in the Asian Indian population (impaired glucose tolerance [IGT] or impaired fasting glucose [IGF] or both). This finding is important as it highlights the need for primary prevention strategies focussing on preservation of beta-cell function and reduction in cell decline.[18]

Increase in beta-cell function and insulin biosynthesis was shown with semaglutide along with improved proinsulin to insulin ratios when compared with other antidiabetic agents including sulfonylureas, which increase insulin secretion with no effect on the biosynthesis of insulin. Also, reduction in insulin resistance was greater with semaglutide vs. placebo, sitagliptin or exenatide extended-release (ER).[19]

Glycemic Efficacy of Oral Semaglutide

Oral semaglutide was effective in reducing HbA1c across the PIONEER trials. In the PIONEER 1 trial, oral semaglutide monotherapy significantly reduced baseline HbA1c compared with placebo after 26 weeks treatment in patients with early T2DM.

In patients with established T2DM who were receiving background oral antidiabetic medications (PIONEER 2-4), 14 mg of oral semaglutide was more effective than empagliflozin 25 mg, sitagliptin 100 mg and similar to liraglutide 1.8 mg at week 26. Flexible dose adjustment of oral semaglutide was more effective than sitagliptin 100 mg for reducing HbA1c at 52 weeks in the PIONEER 7 trial.

In advanced T2DM patients receiving insulin, oral semaglutide significantly reduced HbA1c as compared with placebo at weeks 26 and 52. In patients with moderate renal impairment (PIONEER 5), oral semaglutide 14 mg was significantly more effective than placebo at reducing HbA1c at week 26. In high cardiovascular (CV) risk patients (PIONEER 6), oral semaglutide reduced HbA1c by a mean of –1.0% vs. –0.3% in the placebo group.

Proportion of patients who achieved ADA recommended target of HbA1c <7.0% was persistently greater with

7 and 14 mg of oral semaglutide as compared with placebo and active comparators. Fasting plasma glucose was also generally reduced in patients on oral semaglutide as compared to the placebo and active comparator groups.[20]

OBESITY

Obesity in India is continuously growing and the recent trends indicate a rate anywhere between 13% to 50% of the urban population and 8% to 38.2% of rural population prevalence of obesity. Obesity among Asian Indians has distinctive features like greater truncal, intra-abdominal, subcutaneous and total adipose tissue compared with Caucasians.[21] Several comorbid conditions are associated with obesity like hypertension, hyperglycemia, dyslipidemia, nonalcoholic fatty liver disease (NAFLD), etc. This constellation of conditions is broadly defined as metabolic syndrome.[22]

NAFLD is an important component of metabolic syndrome which can progress to fibrosis and even cirrhosis if there is presence of portal inflammation (nonalcoholic steatohepatitis [NASH]).[23] Approximately one-fourth of urban Indian population has NAFLD and according to a case-control study, Asian Indians in North India with NAFLD have increased adipose tissue, fasting hyperinsulinemia, IGT and metabolic syndrome.[24] The improvement in NAFLD/NASH with GLP-1RAs is thought to be through an indirect mechanism reducing inflammation.[25]

Dyslipidemia is the increased level of total and low-density lipoprotein (LDL) cholesterol, decreased high-density lipoprotein (HDL) cholesterol and hypertriglyceridemia (present alone or together).[26] In Asian Indians with insulin resistance, the plasma adipose tissue metabolites, fatty acids and leptin are higher along with lower adiponectin levels.[27] In a study conducted with oral semaglutide to assess its effects on postprandial glucose and lipid metabolism, it was found that fasting LDL and total cholesterol concentrations were lower with oral semaglutide compared with placebo.

Treatment with oral semaglutide also resulted in lower fasting and postprandial triglycerides than with placebo. In the PIONEER 6 trial, improvements in elevated total cholesterol, LDL and triglycerides, reduced HDL were seen with oral semaglutide. The trial met its primary objective of proving CV safety of oral semaglutide.[28]

Body Weight Reduction with Oral Semaglutide

In the PIONEER clinical trial program, greater number of patients achieved a weight loss of ≥5% across the clinical trials with oral semaglutide 7 and 14 mg (13-44%) versus placebo (3-15%) and active comparators (10-36%) at week 26, which was sustained at the end of trial. Other body size measures like BMI and waist circumference were also reduced with oral semaglutide compared with placebo and active comparators.[20]

ATHEROSCLEROTIC CARDIOVASCULAR DISEASE

According to the Global Burden of Disease study, 24.8% of all deaths in India are associated with cardiovascular disease (CVD). Ischemic heart disease and stroke are responsible for 21.1% of all deaths in India.[29] T2DM and the associated microvascular (retinopathy, neuropathy and nephropathy) and macrovascular (coronary artery disease, peripheral arterial disease and stroke) complications contribute substantially to the morbidity and mortality of the disease. The core pathophysiological mechanism leading to arterial lumen narrowing is atherosclerosis. Recent studies have indicated the central role played by endothelium and inflammation in atherosclerosis.[30]

In animal studies, semaglutide reduced the size of the aortic atherosclerotic plaque lesion independent of its effect on diabetes, body weight and lipids.[25] It is important to note that the findings from the cardiovascular outcomes trial (CVOT) with semaglutide showing effects consistent with reduction in atherosclerotic burden, suggest that the findings seen in animal studies may translate to humans.[14]

The largest cause of diabetes associated morbidity and mortality is CVD. The international diabetology and cardiology guidelines have been updated to put forth a combined approach for the management of T2DM and CVD. The GLP-1RAs or sodium-glucose co-transporter 2 (SGLT2) inhibitors, which have a demonstrated CV benefit are recommended as first- or second-line agents in this regard.

The CAPTURE study found that almost 1 out of 3 adults with T2DM had established CVD. The management of most participants was not according to recent guidelines on diabetes and cardiac disease. There was an unmet need of reducing risk through interventions based on current evidence.[31]

Cardiovascular Safety of Oral Semaglutide

The PIONEER 6 trial was a CVOT designed to establish the CV safety of oral semaglutide; it was not powered for proof of superiority and CV benefit. The investigators concluded the noninferiority of oral semaglutide safety profile to placebo, on a background

of standard care. The CVOT of oral semaglutide to prove superiority in major adverse CV event (MACE) reduction is ongoing as A Heart Disease Study of Semaglutide in Patients with Type 2 Diabetes (SOUL). Pooled analysis, which combined data from CVOTs of oral and injectable semaglutide showed that the once-daily oral and once-weekly injectable showed very similar effects on glycemic and body weight control. Post-hoc analyses suggest a potential for improved CV outcomes with semaglutide irrespective of the route of administration.[32]

HYPOGLYCEMIA

There is a huge corpus of evidence available suggesting that intensive glycemic control with a goal of euglycemia should be instituted as early as possible in diabetic patients. The Diabetes Control and Complications Trial (DCCT) and Stockholm Diabetes Intervention Study (SDIS) showed reduction in the incidence of microvascular complications with intensive glycemic control in type 1 diabetes. The United Kingdom Prospective Diabetes Study (UKPDS) and Kumamoto study found out that tighter glycemic control can delay the onset and progression of micro- and macrovascular complications in T2DM patients.[33-37]

However, due to the risk of hypoglycemia, strict glycemic control is not achieved in majority of patients in real life clinical setting, and this was also a major finding in the above studies. In the DCCT, there was a threefold increase in severe hypoglycemia with intensive therapy as compared with conventional therapy during the study. In the UKPDS, major hypoglycemic episode in a year was significantly higher in the intensive treatment group.[33,35]

The risk of hypoglycemia is increased with insulin excess (exogenous insulin or agents causing release of insulin) and faulty glucose regulation. Progressive beta-cell failure in T2DM increase the severity of hypoglycemic episodes.[37]

Hypoglycemia is a significant barrier to patient adherence to medications leading to suboptimal glycemic control along with the risk of development of complications. Recurrent hypoglycemia worsens the quality of life and can also be fatal.[38]

In a cross-sectional study conducted in an Indian hospital, to find out proportion of T2DM patients reporting at least one or other symptom of hypoglycemia, almost 96% of subjects reported one or the other symptoms of hypoglycemia. Severe hypoglycemia episodes were reported by 19% patients and 8% patients required admission due to hypoglycemia. This study showed the reported prevalence of hypoglycemia among T2DM patients and the urgent need for intervention.[39]

GLP-1RAs have an inherently low propensity to cause hypoglycemia, which was also consistent with oral semaglutide. The PIONEER 4 study was associated with very low proportions of patients experiencing severe or blood-glucose confirmed hypoglycemia (1% and 2% patients, compared with 2% in placebo group). In the PIONEER 8 study, the number of such events was higher in patients having background insulin therapy, but the addition of oral semaglutide to insulin did not increase proportion of patients with hypoglycemia compared to placebo. Most events occurred in patients receiving basal-bolus background therapy with insulin.[40]

CONCLUSION

Oral semaglutide is a revolutionary new drug in the management of T2DM which overcomes the injectable barrier associated with GLP-1RA therapy. It is administered as a co-formulation with an absorption enhancer called SNAC. Oral semaglutide has glycemic control and weight reduction benefits consistent with the GLP-1RA class. India is fast becoming the type 2 diabetes capital of the world with associated conditions like obesity and ASCVD complicating the picture. The pleiotropic benefits of GLP-1RAs are well known and are consistent with oral semaglutide. All the guidelines in diabetes and cardiology have evolved and now recommend a cardiovasculocentric approach to T2DM as opposed to earlier more glucocentric approach.

With oral semaglutide, we have a robust data on the clinical efficacy and safety of oral semaglutide as well as the added advantage of once-daily oral administration, improving patient convenience. The beneficial effects with oral semaglutide like superior glycemic control, weight loss, CV safety and minimal risk of hypoglycemia make it a game-changer for T2DM management in India.

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Failures in the Process of Detecting Pancreatic Cancer Revealed by Researchers

In a recent study, researchers from the United Kingdom revealed how pancreatic cancer tumors are overlooked on computed tomography (CT) and magnetic resonance imaging (MRI) scans, reducing the window for life-saving curative surgery. The study analyzed post-imaging pancreatic cancer (PIPC) cases, where a patient undergoes imaging and fails to get diagnosed with pancreatic cancer but is then later diagnosed with the disease.

The results of the analysis revealed that over a third (36%) of PIPC cases were potentially avoidable, demonstrating a poor detection rate for cancer that has alarming patient outcomes. In the study, 600 patients were enrolled, out of which 46 (7.7%) failed to have their cancer diagnosed through their first scan but then received a pancreatic cancer diagnosis between 3 and 18 months later.

The study results also revealed that in almost half (48%) of PIPC patients examined, there were signs of cancer that had been missed when scans were reviewed by a specialist hepatobiliary radiologist. In 28% of PIPC patients, imaging signs associated with pancreatic cancer, such as dilated bile or pancreatic ducts, were not recognized and investigated further.

Hence, Dr Nosheen Umar, the lead author of the study from the University of Birmingham, UK, commented that the study can raise awareness of the issue of PIPC and the common reasons why pancreatic cancer can be initially missed. This will help to standardize future studies of this issue and guide quality improvement efforts, thereby increasing the likelihood of an early diagnosis of pancreatic cancer. This can increase the chances of patient survival and, ultimately, save lives.

(*Source: https://theprint.in/health/researchers-reveal-failures-in-process-of-detecting-pancreatic-cancer/1162945/*)

Adult Immunization

SANJAY KALRA*, MADHUR VERMA†

ABSTRACT

Vaccination is accepted as an integral part of preventive and community health. However, adult vaccination has not received the same attention as childhood immunization. This communication describes the advantages of adult immunization, and lists high priority populations for the same. It highlights the need to focus on health care workers, sanitation workers and food workers for effective prevention of disease through vaccination.

Keywords: Communicable disease, geriatrics, health care delivery, immunization, vaccination

Immunization has come a long way since 1798, when Edward Jenner developed a vaccine against smallpox.[1] The last century has witnessed multiple advances in the field of vaccines, and immunization is now an integral part of health care. The World Health Organization (WHO) lists vaccines as essential drugs, not only for children and adolescents, but for adults as well.[2] The aim of these vaccines is to prevent communicable diseases, and the morbidity and mortality that may be associated with these diseases.

Globally, and in India, the concept of immunization has gained traction within child and maternal health. The national health programs of India include mandatory vaccines for children and for antenatal women, as part of primary health care provision.[3]

ADULT HEALTH

Adult health, on the other hand, presents different challenges and concerns, as well as obstacles and obstructions. There are multiple fronts to grapple with, including noncommunicable diseases, mental health and trauma. These take up a major chunk of health care resources, and leave little for preventive immunization services. At the same time, however, the evolving landscape of health and diseases offers novel opportunities for the integration and acceptance of vaccination in adults.

Infectious diseases are making a comeback, as exemplified by the recent coronavirus disease 2019 (COVID-19) outbreak.[4] Epidemics and outbreaks of other infections continue to occur in India at regular intervals.[5] Infectious diseases are common in high-risk individuals with impaired immunity. The aging society has also created a large cohort of elderly citizens who are more prone to acute infections. As chronic conditions like lung, heart and kidney disease, as well as diabetes and cancer become more prevalent, the burden of acute comorbid conditions will also increase. All these issues must be addressed to ensure a healthy society.

ADULT VACCINATION

It becomes imperative, to prevent such illnesses, in order to minimize their impact on health and on the health care system. Vaccine preventable diseases (VPD) present a "low hanging fruit" that can easily be tackled with the help of appropriate vaccination.

Rational use of vaccines in adult can help boost the immunity gained from childhood immunization and achieve immunity against other diseases as well.[6] A booster of Td (Tetanus, diphtheria) for children aged 9 to 15 years; one dose of rubella, in previously unvaccinated adolescent girls and women of reproductive age and 2 doses of human papillomavirus (HPV) in adolescent girls are suggested for all immunization programs.[2] Typhoid, cholera, meningococcal, hepatitis A, rabies and dengue vaccines are suggested for some high-risk populations.[2] Mumps, seasonal influenza and varicella vaccines are listed by WHO, but their usage is limited to immunization programs with unique characteristics.

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A few specific populations need special mention in the context of adult immunization. One of these is pregnant women and those planning pregnancy.[7] Women must be protected against all relevant diseases, to ensure a healthy pregnancy outcome. Relevant vaccination should be included in preconception clinics, apart from strengthening antenatal vaccine drives.[8]

Geriatric persons, especially those living in nursing homes or old age homes, should also be prioritized for vaccination.[9] This age group is at greater risk of contracting infections and of developing severe illness due to these. Patients attending specialty clinics for conditions associated with immune compromise, such as diabetes, cancer, chronic liver disease and chronic kidney disease must be a focus of adult vaccination. Persons on long-term glucocorticoid therapy, for pulmonary, rheumatologic or other disease, should also receive extra attention.

HEALTH CARE WORKERS

Health care professionals and providers are the backbone of our health care system. The nature of their job exposes them to various infections that are spread by droplet, blood or touch. Immunization is an effective means of preventing disease in this high-risk category.[10] The WHO recommends polio, measles and annual influenza vaccine for all health workers. BCG, hepatitis B, diphtheria and meningococcal vaccines are recommended for health workers at risk of these infections. Rubella vaccine is recommended for health workers if it has been introduced into the national program. Varicella and pertussis vaccines are listed as optional interventions, keeping health workers as a priority group.[2]

It becomes imperative for the health care system to provide optimal care to its workers. Hence, health care workers should be listed as a separate category in adult immunization policies. Such affirmative action has been noted during the COVID-19 pandemic.

SANITATION WORKERS

While do speak of prioritization of health care professionals for preventive and promotive health strategies, we must not neglect an equally important and perhaps more vulnerable group: our sanitation workers.[11] The nature of their work exposes them to multiple VPD including typhoid, hepatitis A, hepatitis B and rabies. Their work and lifestyle may also make them potential spreaders of such diseases. It would be prudent, therefore, to focus on this group as well. Ensuring that these are vaccinated will lead to a cascade effect on community health.

FOOD WORKERS

Workers in the food industry are potential spreaders of foodborne disease, including typhoid and hepatitis A.[12]

Though no national programs have identified food industry workers as a target population for vaccination, a concerted effort by industry leaders should help in ensuring their immunization against foodborne VPD. This will protect not only the individual workers, but their customers as well. In this way, adult vaccination will benefit the industry and the public at large.

SUMMARY

As we celebrate the successes of our childhood and COVID-19 vaccination programs, it is time to focus on adult immunization. A rational and pragmatic approach to adult vaccination, based upon evidence and economics, will ensure optimization of societal health. Identification of high-risk target audiences, and prioritization of diseases to be targeted, will facilitate efficient use of available resources. Involvement of all stake holders–the public, policymakers, politicians, physicians and payers-will ensure adequate acceptance of, and adherence to, vaccination prescriptions. The Indian Journal of Clinical Practice supports adult immunization as a means of achieving Health for All.

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Poor Outcomes after Fractures in Older Adults Linked to Underlying Health Issues

A study published in the journal *JAMA Network Open* revealed that having specific combinations of underlying health issues is a significant risk factor leading to poorer health outcomes in older adults who have had a prior fracture.

The study conducted by researchers from the Garvan Institute of Medical Research revealed that with fractures closer to the center of the body, a higher mortality rate was observed among older adults in comparison to the general population of the same age.

The findings of the study showed that certain clusters of conditions were associated with increased mortality rates. If older adults with fractures also had multiple or complex health conditions, the mortality risk was higher again.

In the study, chronic health conditions at the time of fracture were naturally clustered into five specific groups for men and four for women: a relatively healthier group with generally only one or no health conditions, a cardiovascular group, a diabetic group, and a cancer group with an additional liver/inflammatory group for men. The presence of specific clusters of health conditions in people compounds the chance of death following these fractures, much greater than either fractures or health conditions alone.

For instance, the mortality rate following hip fracture amongst men in the cancer cluster was 41% higher than that of similarly aged men in the general community. And diabetes in otherwise healthy people was not associated with increased mortality risk, but diabetes in combination with heart, vascular or kidney disease was.

Hence, the study suggested that there's an interaction between the fracture and a patient's cluster of health conditions, including their underlying health, which could be a good way to identify at-risk people.

(*Source: https://www.tribuneindia.com/news/health/underlying-health-issues-linked-to-poor-outcomes-after-fracture-in-older-adults-study-440276*)

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NEW DRUG

Pidotimod: An Immunity Booster

SHUBHRICA*, JYOTI YADAV†

ABSTRACT

Pidotimod is a synthetic dipeptide, which has immunomodulatory property. It is used in recurrent upper respiratory tract infections, where there is nonspecific immune deficiency, especially in children who are more prone to recurrent respiratory infections. This article discusses its structure, pharmacokinetics including mechanism of action and clinical uses. A brief review of literature has been carried out. Possible future application is suggested.

Keywords: Immunomodulators, immunity, immunoglobulin

Acute respiratory infections (ARIs) are the most common infections encountered in pediatric settings and pose a major challenge to the health system in developing countries because of the associated high morbidity and mortality.[1,2] Recurrent respiratory infections (RRIs) present a demanding challenge for pediatricians.[3] ARIs are the infections of any segment of respiratory tract or its accessory structures including paranasal sinuses, middle ear and pleural cavity.[4] But they may not remain confined to respiratory tract and may have systemic effects, due to possible extension of infection or microbial toxins, inflammation and reduced lung function.[5] RRIs can lead to complications such as recurrent otitis media, recurrent infectious rhinitis, recurrent pharyngitis or tonsillitis.[1] RRIs have been generally defined as 3 or more separate episodes of respiratory illnesses or more than 15 days of respiratory symptoms in the past 3 months.[6]

India, Bangladesh, Indonesia and Nepal together account for 40% of the global ARI mortality.[2] In India, 6% of children younger than 5 years of age had symptoms of ARI, i.e., cough, short and rapid breathing and 69% of them availed health care services.[4] ARIs accounted for 30% to 50% of health care visits and 20% to 40% of hospitalizations.[7] An adult has 2 to 4 episodes of ARI/year and a child has 6 to 8 episodes/year. In India, at least 300 million episodes of ARI are estimated to occur every year, out of which 30 to 60 million are moderate to severe ARIs.[4]

Pidotimod is a biological response modifier; chemically it is 3-L-pyroglutamyl-L-thiazolidine-4-carboxylic acid and is unrelated to other immunomodulating agents.[3] Its potential for immunostimulation has been evaluated in conditions with underlying suppressed cell-mediated immunity such as chronic bronchitis and RRIs in children. It is indicated as adjuvant therapy in prophylaxis and management of RRIs including rhinitis, sinusitis, otitis, pharyngitis and tonsillitis. It is also useful in acute exacerbations of chronic bronchitis.

MECHANISM OF ACTION

Pidotimod is a synthetic dipeptide molecule, which exhibits immunomodulatory properties. It exerts its immunomodulating activity by acting on both acquired as well as innate immunity.[3] It affects cell-mediated immune responses by stimulating interleukin (IL)-2 production. Pidotimod increases polymorphonuclear neutrophil chemotaxis and phagocytosis. It also enhances T-cell blastogenesis, anti-CD3 activity and activity of natural killer cells. It also induces maturation and activation of dendritic cells, activation of toll-like receptor (TLR) and release of interferon-gamma (IFN-γ). RRIs have been associated with immunodeficiency conditions like deficiency of immunoglobulin A (IgA), deficiency in cell-mediated immunity (such as total T-lymphocytes, response to mitogens, rosette-forming activity) and decreased neutrophil chemotactic activity and interferon production. It improves or optimizes the impaired T-helper/T-suppressor ratio in children with RRIs.

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ABSORPTION AND DISTRIBUTION

Pidotimod is available in vial, sachets and tablets. The time to peak drug concentration (T_{max}) of pidotimod is 1.5 hours (range 1.3-1.8 hours). After single oral dose of 200 mg, 400 mg and 800 mg in healthy individuals, the mean peak serum concentrations of pidotimod were found to be 2.8, 4.8 and 10.3 μg/mL, respectively. When pidotimod is administered with food, its oral bioavailability is decreased up to 50% and peak serum levels is achieved up to 2 hours later compared to administration in fasting state. Pidotimod should be given 2 hours before or 2 hours after meals to optimize absorption.

It has low protein binding of 4% with a volume of distribution of 30 liters.[8]

METABOLISM AND ELIMINATION

Pidotimod undergoes minimal hepatic metabolism. Approximately 45% of an oral dose (200-800 mg) of pidotimod is excreted unchanged in urine within 24 hours of administration. The total plasma clearance of pidotimod after oral administration is approximately 11 L/hour.

The elimination half-life of pidotimod is 4 hours.[8]

DRUG INTERACTIONS AND ADVERSE EFFECTS

Concurrent or recent use of some drugs like other immunomodulatory drugs, corticosteroids and viral vaccinations may interfere with immunologic actions of pidotimod. It is a generally well-tolerated drug but some very rare side effects such as flushing, rash, pruritus, nausea, vomiting, abdominal pain, diarrhea, headache and drowsiness have been reported.

PRECAUTIONS

Pidotimod should be used with caution in patients with renal failure, diabetes and children below 2 years. It is contraindicated in patients with known hypersensitivity to the components of the formulation. In children aged 2 to 8 years, pidotimod has been used for treatment of acute episodes of RRIs in a dose of 400 mg orally twice daily for 15 to 20 days, in combination with standard antibiotic therapy. A maintenance dose of 400 mg/day, without additional antibiotics has also been used for 60 days, following the acute treatment phase. For prophylaxis of RRIs in children of 2 to 13 years of age, pidotimod is usually given orally at dose of 400 mg once-daily before breakfast for 60 days. A twice-daily regimen of pidotimod 400 mg for 15 days, followed by once-daily maintenance dose, has been used to rapidly improve immune response.

USE IN SPECIFIC POPULATIONS

In adult patients with renal impairment having serum creatinine 2 to 5 mg/dL, the elimination half-life of pidotimod is prolonged up to 8 hours and its clearance reduced (mean 1.6 L/hour) following intravenous administration. Considering the usual dose interval of oral therapy (once or twice daily), it may not be necessary to reduce dose in these patients. However, additional repeat dose studies with oral dosage forms in patients with varying degrees of renal insufficiency are needed to confirm this recommendation. Pidotimod may prevent RRIs in children.[9] Immunomodulatory activity of pidotimod administered with standard antibiotic therapy in children hospitalized for community-acquired pneumonia has been observed.[10] Pidotimod may prevent ARIs in healthy children entering into daycare.[11]

POSSIBLE FUTURE APPLICATIONS

Pidotimod has shown improvement in symptoms; hence, it may be considered for use in ambulatory adult COVID-19 patients without pneumonia to prevent worsening of symptoms. However, more studies are needed to confirm these observations.[12]

CONCLUSION

Pidotimod has immunomodulatory action. It has been shown to be effective in reducing ARIs and reducing their severity among children who suffer from RRIs. It may also be beneficial in preventing ARIs in healthy children attending daycare centers. In hospitalized patients with acquired pneumonia, pidotimod is associated with favorable and persistent immunomodulatory effect when used along with standard antibiotic therapy. Overall, pidotimod is safe and has good tolerability.

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■■■■

Women are at Higher Risk of Lung Cancer Than Men

In recent years, pollution and other factors in India have led to a troubling trend of greater lung cancer rates in women than men. The findings further showed that smoking rates remained stable even when the percentage of female lung cancer patients grew. The All India Institute of Medical Sciences (AIIMS) in Delhi hosted the study, which spanned 10 years from January 2008 to March 2018.

Historically, lung cancer has been more common in men than in women. Still, the pattern seems to be shifting in numerous regions of the world in recent years, according to Dr Anant Mohan, Head of the Department of Pulmonary Medicine at AIIMS. The causes were alteration in smoking behaviors, exposure to environmental toxins and biomass, particularly in rural women. But the improved access to health care facilities had encouraged more women to seek medical attention Dr Anant stressed.

The recently unpublished study by the pulmonary department showed that non-tobacco exposures such as indoor air pollution, poor environmental quality or urban air quality might have a role in women's rising trend of lung cancer. The study found that squamous cell carcinoma (SCC) increased from 25.4% to 30.6%, while adenocarcinoma (ADC) increased from 9.5% to 35.9%. Better survival rates were found among the nonsmokers, those who were younger, primarily women and more educated. They also had a higher prevalence of ADC, epidermal growth factor receptor (EGFR) and anaplastic lymphoma kinase (ALK) mutations.

(*Source: https://health.economictimes.indiatimes.com/news/industry/lung-cancer-rates-higher-in-women-than-men-study/94772766*)

CASE REPORT

Crigler-Najjar Syndrome Type 2 in an Adult: A Rare Presentation

SOURABH SONI*, ANIL SAMARIA†, MEENAKSHI SAMARIA‡, MONIKA CHOWDHARY#, AMIT KANT*, DEEPAK DEWAT*, NK MAHESHWARI¥

ABSTRACT

Introduction: Crigler-Najjar syndrome type 2 (CNS type 2) is a rare disorder that causes elevated levels of bilirubin in the blood (nonhemolytic unconjugated hyperbilirubinemia). The main symptom of CNS type 2 is persistent jaundice. It is caused by genetic changes in the *UGT1A1* gene and the inheritance is autosomal recessive. Genetic testing of the *UGT1A1* gene for mutations is the diagnostic clincher. We report one such rare case. **Case report:** A 75-year-old male presented with history of right-sided weakness with right-sided facial weakness, MRI brain revealed an infarct in the left side of brain with general physical findings suggestive of icterus. **Conclusion:** Diagnosing and managing these patients may be challenging. Our aim is to draw attention of the treating physicians towards this disease with the help of this case report.

Keywords: Crigler-Najjar syndrome, isolated indirect hyperbilirubinemia

Crigler-Najjar syndrome (CNS) is an inherited hyperbilirubinemia syndrome, characterized by isolated unconjugated hyperbilirubinemia. Type 2 CNS also known as Arias syndrome, named after the physician who first described it in 1962, Crigler-Najjar type 2 is somewhat more common than type 1. Patients live into adulthood with serum bilirubin levels of 6-25 mg/dL.[1] In these patients, mutations in the bilirubin uridine diphosphate-glucuronosyltransferase (UDPGT) gene cause reduction—typically ≤10%—of the enzymatic activity.

Bilirubin UDPGT activity can be induced by the administration of phenobarbital, which can reduce serum bilirubin levels in these patients. Despite marked jaundice, these patients usually survive into adulthood. The prevalence of CNS type 2 is not known but an approximate annual incidence of 1 per million live births has been found in case reports from worldwide for both the types of CNS.[2] It is differentiated facilely from its doppelgangers-hemolytic syndrome and Gilbert's syndrome in which bilirubin levels rarely cross 6 mg/dL.[3] In this article, we present a case of CNS type 2 in an adult as it is a rare disorder, and therefore, it is important to draw attention towards such cases.

CASE REPORT

A 75-year-old male presented to the emergency department of our hospital with complaints of right-sided weakness along with right-sided facial weakness. The patient was a known case of type 2 diabetes mellitus and ischemic heart disease. Detailed history revealed that the patient had yellowish discoloration of both the eyes since childhood. The patient was the 7th brother among 8 siblings; all the brothers had a similar history of yellowish discoloration.

On examination, the patient was conscious and oriented to time, place and person. On head to toe examination, the patient had icterus (Fig. 1).

Figure 1. Patient's eyes showing presence of icterus.

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On central nervous system examination, the patient had normal higher mental functions. The right side upper limb had power of 3/5 and the lower limb had power of 3/5, brisk deep tendon reflexes. The right-sided plantar reflex was extensor. On cranial nerve examination, the patient had right-sided upper motor neuron type facial nerve palsy.

An early diagnosis of right-sided hemiparesis with right-sided facial nerve palsy with hyperbilirubinemia was made. The noncontrast computed tomography (NCCT) head obtained initially showed no signs of infarct. The magnetic resonance imaging (MRI) brain on the other hand revealed left-sided infarct.

The biochemical assessment showed total bilirubin levels of 17.6 mg/dL with direct bilirubin levels of 0.2 mg/dL, serum glutamic oxaloacetic transaminase (SGOT) - 27.0 U/L and serum glutamic pyruvic transaminase (SGPT) - 14.4 U/L; other biochemical investigations were within normal limits. There were no markers suggestive of hemolysis. The viral markers for viral hepatitis were negative. The patient was unwilling for liver biopsy. Hence, a provisional diagnosis of CNS type 2 was made after ruling out other causes of isolated hyperbilirubinemia. *UGT1A1* gene polymorphism test by PCR fragment analysis revealed Genotype **28/*28* with 2 alleles each with 7 TA repeat (7/7 homozygous) demonstrating severely reduced glucuronidation activity. The other causes of unconjugated hyperbilirubinemia were ruled out.

The patient was treated with antiplatelet agents along with statin therapy, and advised follow-up.

DISCUSSION

As a differential to unconjugated hyperbilirubinemia, CNS is a rare genetic disorder, which is defined by impaired conversion and clearance of bilirubin.

During normal reaction bilirubin produced by the lysis of heme is converted from an unconjugated form to a conjugated form, which dissolves in water and is be excreted out of the body. The patients affected with this syndrome have trouble in converting unconjugated bilirubin into the conjugated form because they lack a specific liver enzyme required in the metabolism of bilirubin. Since there is no conversion of bilirubin, this results in abnormally high levels of unconjugated bilirubin in the blood (unconjugated hyperbilirubinemia).

The defining feature of CNS is a persistent yellowish discoloration of the skin, mucous membranes and sclera (jaundice).

CNS is of two types: CNS type 1, characterized by a nearly complete lack of enzyme activity and severe, potentially fatal symptoms; and CNS type 2, a result of reduced enzyme activity and mild symptoms.

Our patient presented at 75 years of age, but he had developed clinical features of icterus since birth, which is consistent with age group within which this disease usually manifests. He also presented with right-sided hemiparesis and facial nerve palsy. The higher mental functions were normal. No other biochemical abnormalities suggestive of any other hepatobiliary disease were detected. *UGT1A1* gene study revealed reduced enzymatic activity. The patient upon detailed history also revealed history of similar illness in all siblings.

The icterus in CNS type 2 persists since early childhood and it is often not associated with kernicterus like features.

The pattern for inheritance for both subtypes of CNS is as autosomal recessive traits and are caused as a result of errors or mutations of the *UGT1A1* gene.[4]

CNS type 2 is usually managed conservatively with avoidance of drugs that displace bilirubin from albumin such as ceftriaxone, furosemide, penicillin, sulfonamides, salicylates. The dose of phenobarbitone preferably used is 60-180 mg/day in single or divided doses.[5] The response occurs within 2 to 3 weeks of administration. It is preferred to be given lifelong even though there are minimal symptoms. Clofibrate (2 g/day in divided doses) has also been proved to be equally efficacious. Calcium supplementation has also been found to increase the gut excretion of bilirubin. Plasmapheresis or phototherapy are reserved to deal with a hyperbilirubinemic crisis. Lifelong phototherapy is required rarely.

CONCLUSION

Crigler-Najjar syndrome type 2 is rare genetic disorder of bilirubin metabolism and a rarer cause of jaundice in an adult. A high level of clinical suspicion based on some of its unique features can aid diagnosis. Hence, a patient presenting with asymptomatic indirect hyperbilirubinemia that patient should be evaluated for CNS as a potential differential diagnosis.

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Contributions: SS prepared the draft manuscript under the guidance of SA, SM, CM, MN. Final manuscript was read and approved by all authors for submission.

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Consent for Publication: Written and informed consent was obtained from patient's wife as well as father for publication of this case report and any accompanying images which do not include the patient's photograph.

Conflict of Interests: The authors declare that they have no conflict of interests.

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■■■■

Hair Cortisol: A Potential Biomarker of Stress?

Measuring the hair cortisol level may be indicative of psychological stress, suggests a study published in the journal *PLoS Global Public Health.*[1]

To analyze the association between hair cortisol concentration (HCC) and perceived stress, hair samples were obtained from 398 women from the Icelandic stress and gene analysis (SAGA) pilot-cohort and 881 from the Mexican Teachers' Cohort. The hair samples were collected from the back of the head (posterior vertex). "As hair grows an estimated 1 cm per month, the 3 cm closest to the scalp represent the prior 3 months", note the authors.

The hair cortisol levels, measured by liquid chromatography and tandem mass spectrometry, were higher among the Mexican participants compared to the Icelandic women; 6.0 pg/mg vs. 4.7 pg/mg (median), respectively. They also had higher psychological stress as assessed by the self-reported Perceived Stress Scale (PSS, 10 and 4 item, range 0-40 and 0-16); 12.4 vs. 11.7, respectively. When the Mexican and Icelandic women were examined as one group, it was found that for every unit increase in the PSS-10 score, the hair cortisol levels increased by 1.45 after adjusting for behavioral, social and demographic factors. The cortisol levels increased by 24.3% from the lowest to the highest quintile on the PSS scale.

This study has linked hair cortisol concentration and perceived stress in two diverse groups of participants in a linear association. The levels were higher among women who scored the highest on the PSS. This association remained unchanged even after adjusting for multiple variables, "though the absolute difference was small".

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CASE REPORT

Stroke – A Rare Initial Presentation of Takayasu Arteritis

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ABSTRACT

Introduction: Now-a-days, young people below age of 40 years without known risk factors are presenting with stroke. The cause of stroke should be found so that recurrence and other complications can be prevented. **Case description:** An 18-year-old female presented with holocranial headache, focal seizures with impaired awareness and left hemiparesis. The upper limb pulses were absent on both sides, while pulses in lower limbs were present. MRI scan of brain revealed infarct in right middle cerebral artery territory. CT angiography brain showed luminal narrowing in upper limb arteries, carotid artery and vertebral artery. She was treated with antiplatelet drug, tablet carbamazepine, tablet methotrexate with folinic acid and she improved. **Discussion:** Takayasu arteritis is an inflammatory vasculitis disease causing stenosis in medium and large sized arteries. It can present as stroke, myocardial infarction, aortic insufficiency, retinal ischemia, renal failure and hypertension. **Conclusion:** Takayasu arteritis is one of the rare causes of stroke, which when detected should be promptly treated to prevent further episodes of stroke and other system complications.

Keywords: Stroke, Takayasu arteritis, vasculitis

Takayasu arteritis is a large vessel vasculitis, which mostly affects the aorta, carotid arteries and renal vessels. Takayasu arteritis usually presents with fever, myalgia, night sweats, arthralgia and absence of peripheral pulses. Despite luminal narrowing of large vessels, it rarely presents with stroke as an initial presentation. Patients commonly present with limb claudication, coronary artery disease and renal hypertension.

METHODS

Detailed history and clinical examination of the patient was done. Blood investigations, i.e., complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), renal function test, ANA (antinuclear antibody) profile was done. Radiological investigations, i.e., ultrasound of neck, arterial Doppler of upper limbs and lower limbs, computed tomography (CT) angiogram of brain, chest and abdomen and magnetic resonance imaging (MRI) of brain was done. Case was discussed with Rheumatologist regarding disease-modifying medications to prevent future relapse. Informed consent was taken from the patient.

CASE DESCRIPTION

An 18-year-old female presented with holocranial, dull aching headache aggravating on coughing and bending forward for 2 days. On the third day of her illness, she had 1 episode of focal seizures involving left upper and lower limb, up rolling of eyes, followed by post-ictal confusion lasting for 3 minutes. It was followed by weakness of left upper and lower limb. There were no associated previous comorbidities. There was no similar history in the family members.

On general examination, pulses were absent in both the radial and brachial arteries; both carotid pulses were weak. She had left upper motor neuron type of facial palsy, left hemiparesis with power 3/5, deep tendon reflexes 2+ in all 4 limbs, with plantar-extensor on left side with circumduction gait. Her sensory, cerebellar, autonomic systems were normal.

Her blood work-up showed hemoglobin - 9.6 g/dL, total leukocyte count (TLC) - 10,200/cumm, TPC - 3,92,000/cumm, normal renal function test, ANA

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profile - negative, HIV test - negative, ESR - 100 mm/hr, CRP - negative, ultrasound neck - steno-occlusive disease in bilateral carotids.

MRI of brain showed acute infarct in right frontal lobe, right caudate nucleus, lentiform nucleus and right corona radiata (Fig. 1). Magnetic resonance angiogram (MRA) of intracranial vessels showed nonvisualization of intracranial part of right internal carotid artery and complete reformation of right anterior cerebral artery (Fig. 2).

Arterial Doppler of upper limbs showed significant stenosis in the proximal subclavian artery. CT angiogram of brain (Fig. 3) and chest (Fig. 4) showed complete occlusion of right common carotid artery and 50% occlusion of left common carotid, 20% to 30% luminal narrowing of both internal and external carotid artery, occlusion of left and right vertebral artery, both subclavian artery occlusion (30% occlusion), both axillary, brachial, radial, ulnar artery and descending thoracic aorta (20% occlusion). Renal arteries, abdominal aorta, external and internal iliac arteries on both sides were normal.

She met 3 out of 6 American College of Rheumatology (ACR) criteria. She had type IIB Takayasu arteritis.

She was treated with injection dexamethasone 8 mg BD, injection levetiracetam 500 mg BD and tablet aspirin 150 mg OD. Tablet methotrexate 7.5 mg once a week was started as advised by the Rheumatologist. Her power improved with minimal deficit. She was discharged with tablet methotrexate 7.5 mg once a week, tablet

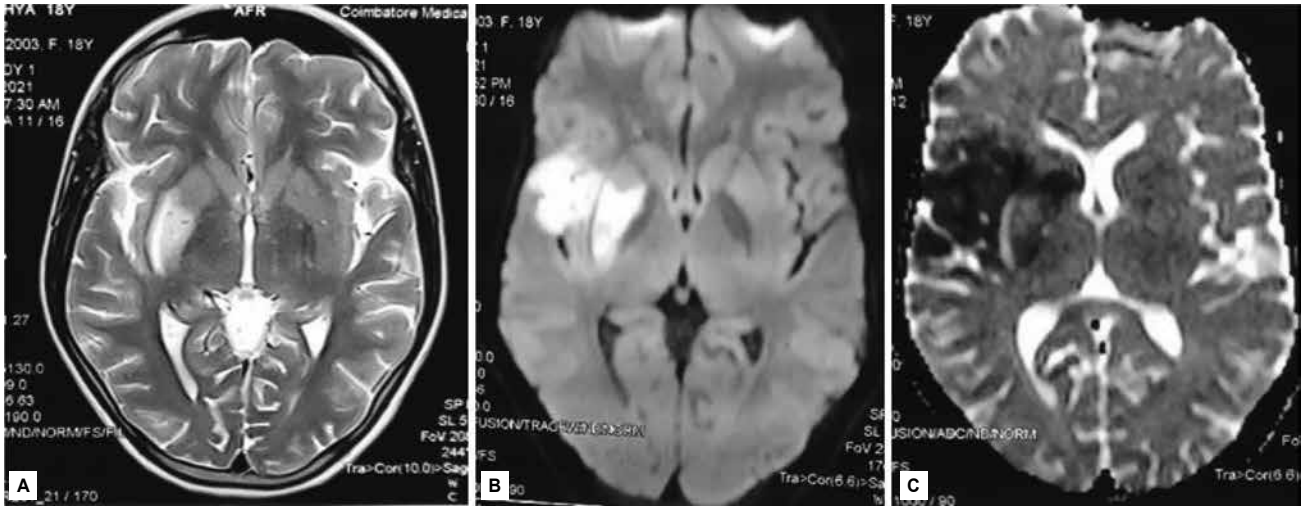

Figure 1. MRI of brain – **A)** T2/FLAIR; **B)** Diffusion-weighted imaging showing hyperintensity in right insular cortex and right lentiform nucleus; **C)** Attenuated diffusion coefficient showing hypodensity in the right gangliocapsular area, right insular cortex and caudate.

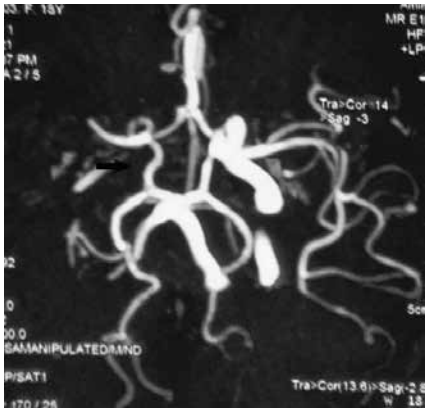

Figure 2. Magnetic resonance angiogram – right middle cerebral artery not visualized.

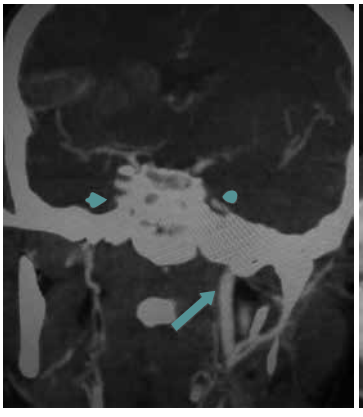

Figure 3. CT angiography of brain – Nonvisualization of infraclinoid part of right internal carotid artery, nonvisualization of right common carotid artery.

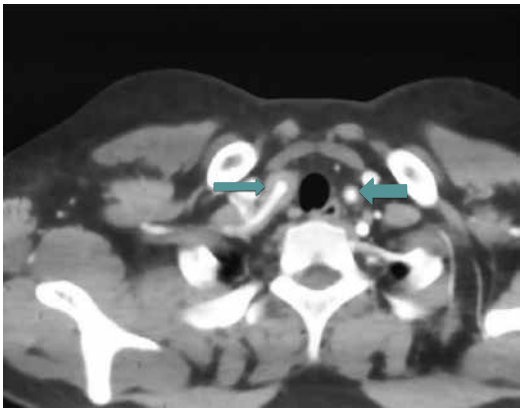

Figure 4. CT angiogram of chest blood vessels – mural thickening seen in both the subclavian arteries.

prednisone 20 mg, tablet aspirin 150 mg BD and tablet levetiracetam 500 mg BD, tablet folic acid 5 mg OD. On follow-up, she is doing well with no further episodes.

DISCUSSION

Takayasu arteritis is a large-vessel vasculitis of unknown cause affecting females aged 11 to 30 years. It affects aorta, carotid artery, renal and pulmonary artery and causes formation of thrombus leading to stenosis and obstruction of the blood vessels. The complications of Takayasu arteritis are vascular claudication, renal hypertension, congestive cardiac failure and coronary artery disease. Stroke occurs in 10% to 20% of cases having Takayasu arteritis. Possible cause of stroke in Takayasu arteritis include embolism from stenotic or occlusive lesions in the aortic arch and its main branches.[1-3]

For diagnosing Takayasu arteritis as the cause of the stroke, 1990 ACR criteria was used, according to which the patient should have at least 3 out of 6 criteria:

1. Onset at age of 40 years or younger
2. Claudication of an extremity
3. Decreased brachial artery pulse
4. Difference higher than 10 mmHg in systolic blood pressure between arms
5. Presence of a bruit over the subclavian arteries or the aorta
6. Arteriographic evidence of narrowing or occlusion of the entire aorta, its primary branches or large arteries in the proximal upper or lower extremities.[2]

The patient had type IIB Takayasu arteritis, which was concluded from the following 6 types based on angiographic involvement:

- Type I – Branches of the aortic arch
- Type IIa – Ascending aorta, aortic arch and its branches
- Type IIb – Type IIa region plus thoracic descending aorta
- Type III – Thoracic descending aorta, abdominal aorta, renal arteries or a combination
- Type IV – Abdominal aorta, renal arteries or both
- Type V – Entire aorta and its branches.[4]

The inflammatory process of vasculitis in Takayasu arteritis is mediated by T cells, macrophages and dendritic cells in the arterial wall. The inflammation starts in tunica media and adventitia followed by panarteritis. The aortitis leads to extensive fibrosis and increased wall thickness.[1,2,5]

On clinical examination, patients have loss or inequality of pulses in the upper limbs (known as *Pulseless disease*), asymmetric blood pressures between upper limbs or bruits heard in neck, supraclavicular region.[1,2]

Ultrasound Doppler of arteries, CT of brain, CT angiography and MRI of brain are the radiological modalities that help in diagnosing Takayasu arteritis and tell us about the affected vessels. Steroids are the first-line treatment. For long-term treatment, steroid-sparing drugs are used, i.e., methotrexate, cyclophosphamide, azathioprine. The patient should be started on immunomodulatory drugs to prevent the progression of the disease and to reduce the further involvement of the other unaffected blood vessels.[6]

Prognosis and recovery are good, with stable course of the disease on immunosuppressive therapy.[6-8]

CONCLUSION

Complete clinical examination and prompt evaluation of the cause of stroke in young patients can help in reducing morbidity and early rehabilitation to led a better quality of life. Proper guidance about Takayasu arteritis and continuation of immunomodulatory therapy can help these patients in avoiding future complications.

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Safeguarding Our Adolescents from Inappropriate Use of Smart Gadgets: Hacks and Heuristics

MEENAKSHI VERMA*, SUNEET KUMAR VERMA†

ABSTRACT

Adolescents (children aged 11-19 years) are at the greatest peril when it comes to use of smart gadgets. These gadgets are essential for literacy and development, but also have the potential to cause addiction and other unwanted effects. Finding the right balance is the key. Thus, there is a considerable need to devise, enlist and convey to parents, various hacks and heuristics that can be used by them to optimize the use of smart gadgets by their teenager children. This communication should prove helpful for all health care professionals who are directly or indirectly involved in adolescent health care.

Keywords: Screen addiction, adolescent health, counseling, digital health, pediatric health, psychology, screen time, teenagers

Adolescent age is a very fragile phase in a human being's life span. At this age, one is neither mature enough to differentiate wrong from right nor is one so trusting as to unquestioningly abide with rules set by parents. Adolescence is a vital phase as the future personality of a person depends largely on the habits imbibed during this phase.[1] One such habit that affects the adolescents' future in the long run is inappropriate use of gadgets.[2] They are extremely vulnerable to be influenced by the content of the media shown and to be exploited by cyber-bullies. Nevertheless, it's very difficult in this current tech-based world to just seize their gadgets authoritatively and restrain them from e-communication. If we as adults can't imagine staying away from our phones for a day, how can we expect our younger generation to do so? Just think about it.

We are privileged to be living in an era where we can reach every corner of the world in just a blink of an eye! The younger generation has equal rights to experience this privilege. Denying them of this 'new normal' would only make things worse. Moreover, the compelling digitalization of education system during the COVID pandemic has strengthened this normalcy further.[3]

The need of the hour is not to devise ways to keep the teenagers away from screens but to concoct a systematic course of action to let these screens turn into a helping tool for their better personality development. The hacks and heuristics as enumerated in Table 1, can help to raise an adolescent into a real human reflecting a technology driven personality with a realistic human touch.

PARENTING MEANS COMMUNICATION

The responsibility to safeguard the adolescents from the dangers of screen addiction lies equally on the shoulders of parents as well as health care professionals. Parents must fetch time to *communicate* with their adolescent children to keep the parent-child relationship strong during this tricky age.[4]

Just half an hour of daily conversation by either of the parents is enough to let them realize the bond shared. That must include some general talks about life, knowing about their friends and teachers, their career choices, involving them in family decision making and simultaneously fetching information about their current social media ventures. Explain the dangers of too much of screen time and keep reinforcing the same. We can call it as *friendly parenting*. This is the only way to win the trust of an adolescent soul. At this age, they

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Table 1. Hacks and Heuristics to Safeguard Adolescents from Inappropriate Gadget Use

General rules of parenting
• Face-to-face communication
• Friendly parenting
• Planning an excursion
• Engaging in a sport of interest
• Extracurricular skill
• Competitiveness
• Protective strategies
• Pre-sleep ritual
• Actions right from the childhood
Rules related to e-communication
• Digital literacy
• Right time to own personal device
• Family social media group
• Vigilance for screen or game addiction
• Family screen rules
• Screen-free timings and zones

need an unconditional support from their parents to avert themselves from falling prey to the fallacies of virtual world. That is possible only if the level of trust between the parent and child is too strong to hide anything. The responsibility of a parent must never fall short even if the child is adamant or stiff-necked. Tackling such a stubborn child is although difficult, but not impossible. Consistent communication is the key to turn the tide. Never forget the following rules while talking to them: listen, show trust and understanding, validate their feelings, respect their ideas, avoid being a dictator, praise often, control your emotions and be observant.[5]

DIGITAL LITERACY

Digital literacy holds a crucial space in today's globalized scenario. Acquisition of digital skills is one of the basic aspects of education now-a-days. These skills are mandatory to live in a society where access of information is mainly through technology.[6] It also includes teaching them how to use technology effectively and safely. It can be provided both by schools as well as at home by joining professional digital education courses once a week. Getting indulged into an entirely different digital space makes them less vulnerable to be trapped in cyber-crimes. Moreover, their career opportunities would also increase astronomically.

SOCIAL LITERACY

Apart from the above indoor tasks, adolescents should also be encouraged to explore the outside real world. This can be achieved by planning a *family excursion* at the weekends to rejuvenate their mind and body. Leaving all the mobile phones and gadgets back home would definitely be an icing on the cake. The adolescent children are stocked with relentless energy. This fact can be utilized to divert their attention away from the screens by enrolling them into any *sport of their interest*. This would keep their physical fitness at par as well as would lead to a shift of focus from worthless online concoctions to a more valuable pursuit.[7]

Additionally, there are a vast variety of *extracurricular skills,* which are equally helpful in rerouting the nerves of young brains, like singing, dancing, playing a musical instrument, painting, photography, craft, pottery, martial arts, story writing, learning second language, etc. As soon as the child seems to develop even a slight interest in any of the skill or activity, he/she should be encouraged to pursue the same. The key is to provide the spark at the point of ignition itself and the aim is again to safeguard them from unnecessary use of internet.

Having them engaged into the above-mentioned activities; an effective hack is to inculcate *competitiveness* with their peer groups with respect to the concerned sport or activity as well as in the academic feats. The young ambitious minds won't mind trading their screen time for skill practice and studies to outperform their competitors.

E-CHAPERONING

There comes a time when an adolescent is ready to have a *personal smart device*, something which ought not to be denied.[8] The onus of choosing the right time is on the parents. Once they have developed a trustworthy friendly relationship with their child and are confident enough to implement proper *protective strategies*, the time has arrived. The strategies include keeping a watch on search history, scrutinizing the apps used, performing extensive research of the video games played, making them aware of cyber-crimes, teaching them the importance of password protection of social media accounts, making them wary of downloading unnecessary utilities or data, not allowing them any online mode of payment, etc.

Once they have mobiles of their own, they should be added into the *family social media group* to inculcate in

them a sense of being an important member of the family. Sharing important family discussions, forwarding meaningful quotes and inspirational videos, chatting about current affairs, are some of the activities which would increase his sense of responsibility towards the family and society.

Family screen rules still play an important role in curbing most of the habit-forming actions. The rules must be abided by all the members of the family invariably. Setting an example yourself will convince them more to follow the suit. Manage your own screen time first. Certain *screen-free zones* at home, like the dining area, the bed, the play area, allow the child to understand the family values. For that matter, displaying the *screen-free zone* stickers at these areas inculcates a sense of compulsive discipline.

Lastly, a *pre-sleep ritual* must be followed invariably every day, a time which must be reserved for the family fun together.[9]

SCREEN ADDICTION

With every beautiful phase of life, the likelihood of insecurity prevails. *Screen addiction* is one of the most atrocious byproducts of adolescents owning personal smartphones. One must be vigilant in recognizing early signs of the same. Finding the child often seeking for lonely space at home, avoiding family get-together moments, complaining about being bored often, being unhappy during screen-free times, showing agitated behavior when asked to stop mobile use, being absent-minded, declining academic performance, increasing oppositional behavior, dull looking face, dark under eye circles, are some of the symptoms, which when observed must be immediately attended to before it gets too late.[10] Similar are the signs of online game addiction or traps, which also include unusual aggressive behavior, constantly asking for activation of payment modes, giving up extracurricular activities, remains preoccupied with video games, becoming emotional when video game apps are removed and an inability to control the urge to play. This internet gaming disorder is the worst that can happen to a child. It becomes mandatory to consult a child psychologist to timely provide cognitive behavior therapy. Else, prevention is better than cure.

SUMMARY

The above-mentioned strategies would work best if the implementation starts *right from the childhood*. Growing into a competent human being, capable enough to lead a successful life at par with the existing technology, has remained a constant goal for children of all times. Today's technology driven world demands an additional constitutional reform in terms of right to use the gadgets by children in an age appropriate manner and in accordance with the required developmental stage of the child.

The hacks and heuristics that we share in this article will go a long way in ensuring that this right is met, in a responsible manner.

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VIEWPOINT

Democracy in Diabetes Care: Acting Upon the Three A's – Accessibility, Affordability and Awareness

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ABSTRACT

Diabetes care is the right of every individual living with diabetes. In this communication, we describe the epidemiology of diabetes in India, draw parallels between democracy and diabetes, and call for the democratization of diabetes care. We highlight the three A's – Accessibility, Affordability and Awareness—that are essential for democratic diabetes care and share best practices towards this end.

Keywords: Diabetes, patient-centered care, person-centered care, type 1 diabetes, type 2 diabetes

The prevalence of diabetes is out of control. Previously thought to be a disease of the affluent "Western" nations, type 2 diabetes has spread globally and is now a leading cause of disability and mortality, impacting even younger age groups. At least 537 million people live with diabetes across the globe, and this number is expected to rise to 783 million by 2045.[1]

To add to this, 3 in 4 people with diabetes live in low- and middle-income countries. In India, diabetes has risen from 7.1% in 2009 to 8.9% in 2019.[2] India ranks second with 74.2 million people living with diabetes, which is expected to rise to 124.9 million by 2045.[1] Of these, 53.1% are undiagnosed. India has the third-highest (0.6 million) annual deaths due to diabetes, after China and the United States.[1]

A large community-based study in North India (STEPS survey) showed that out of 5,127 diabetes patients, 18%, 51% and 31% were in the age groups 18-24, 25-44 and 45-69 years, respectively; however, the prevalence of diabetes mellitus was found to be significantly higher among those aged 45-69 years (18.0%).[3] An increase in the prevalence of patients with diabetes (≥20 years) was reported in 2016 (7.7% [6.9-8.4]) compared to 1990 (5.5% [4.9-6.1]).[4]

According to several studies, the burden of diabetes is shared differently by genders due to various factors.[5] Studies in northern India show that women are more likely to develop diabetes, whereas those from southern India show that males are more likely to be diagnosed with diabetes.[6] Researchers have examined socioeconomic disparities in diabetes prevalence, but the gender disparity has not been investigated.[7] Few other studies have focused either on a single state or the geographical variation in the prevalence of diabetes in the country.[8]

The *India State-Level Disease Burden Initiative Diabetes* study reported the highest prevalence of diabetes in Tamil Nadu, followed by Kerala, Delhi, Punjab, Goa and Karnataka.[4] Another study showed that states with higher per capita gross domestic product (GDP) and those belonging to higher socioeconomic status had more diabetes cases. This led to a clear epidemiological transition with a higher prevalence of diabetes in the low section of urban areas in the more economically developed states.[9]

According to the DIABetes study, the largest nationally representative epidemiological survey of India (data from 15 states/union territories), diabetes prevalence ranged from 3.5% to 8.7% and 5.8% to 15.5% in rural and

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urban areas, respectively, with the figure ranging from 4.3% in Bihar to 13.6% in Chandigarh.[10] This indicates that the prevalence of diabetes was higher in urban areas (11.2%) than in the rural areas (5.2%).[10]

THE RESPONSE

Weak public health systems have been identified as a significant hindrance in providing quality diabetic care in low- and middle-income countries. Under the National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS), as part of the National Health Mission (NHM), Ministry of Health & Family Welfare, the Government of India focuses on strengthening infrastructure, equipment, human resource development, health promotion and awareness generation for prevention, early diagnosis, management and referral to an appropriate level of the health care facility for treatment of the noncommunicable diseases (NCDs).[10] Under NPCDCS, 682 district NCD clinics, 191 district cardiac care units and 5,408 community health center NCD clinics have been set up across India. A total of 7,04,631 Accredited Social Health Activists (ASHAs), 2,19,113 Auxiliary Nurse Midwife (ANM)/ Multipurpose Workers (MPW), 28,912 staff nurses, 76,567 Community Health Officers (CHOs) and 29,648 Medical Officers (MOs) have been trained on universal screening of common NCDs.[10] Besides the government infrastructure stated above, multiple private diabetes care set-ups, varying from small diabetes clinics to corporate hospitals and chains of diabetes care clinics are taking care of diabetes patients across the country.

THE RESULT

Despite these resources, 3/4th of the Indian population (76.6%) had poor glycemic control (glycated hemoglobin [HbA1c] ≥7%), as reported by a large real-world study (n = 55,633 type 2 diabetes mellitus [T2DM] patients). In this study, one-third of the patients had microvascular complications.[11] To add to this, the ICMR-INDIAB study found that only 31% of persons with self-reported diabetes had an HbA1c below 7%. More than 60% of patients had not checked their HbA1c in the past year.[9]

The major challenges in achieving glycemic targets are clinical inertia, poor drug adherence and low disease awareness. Poor adherence can be because of the cost of the treatment, accessibility to health care or lack of awareness. Self-monitoring of blood glucose (SMBG) levels and enhancing medication adherence can contribute to meaningful improvements in HbA1c control.[12] Additionally, the quality of diabetes management in India varies considerably with physicians' awareness levels, attitudes and perceptions of diabetes care.[13]

THE RIGHT

In this scenario, we look towards our great Indian Constitution for guidance. It lays out every citizen's fundamental rights and duties. Although it does not explicitly define the "Right to Health", several references are made about public health that can serve as a beacon of hope toward universal health care. The Apex Court reaffirmed that every citizen of India has the right to health. Consequently, the "Right to Diabetes Care" is under this obligation and should be provided to every citizen, ensuring it is accorded affordably and appropriately.

Parallels can be drawn from the Constitution towards diabetes health care against the backdrop of the three values that the constitution assures its citizens – justice, equality and liberty. These can serve as the basis for driving a change around making diabetes care universal. Justice, in the diabetes care scenario, would imply offering the correct screening, diagnostic, monitoring and therapeutic tools to all those in need. Equality would mean that all people seeking health care be treated equally, without discrimination on any grounds. Liberty supports the right to freedom in patient-centered care (PCC) and patient autonomy. PCC is "providing respectful care and responsiveness to individual patient preferences, needs and values and ensuring that patient values guide all clinical decisions."

Every citizen of India must be accorded the right to euglycemia. It is not just the biochemical parameters but a holistic approach. It is about creating an environment conducive to promoting euglycemia by encouraging appropriate individual and community lifestyle and diet changes. It is paramount that the model is sustainable, self-sufficient, universal and patient-centric.

THE THREE A'S

Utilizing the principles behind the three values as enshrined in our constitution, we should aim towards the right to euglycemia, following a path built on the 3A's – Accessibility, Affordability and Awareness. These would ensure that each citizen of India is provided with genuine quality diabetes care irrespective of economic stature, social standing, educational background, age, gender, etc.

Accessibility

Accessibility to diabetes care is hampered because of the high patient-to-provider ratio and geographical location, particularly in rural areas where people have to travel several hours to get their investigations done or consult a specialist. Management of T2DM in low- and middle-income settings is suboptimal due to less access to medications, comorbidities and the growing population of patients, which is responsible for the overuse of existing resources.[14] There are often delays in diagnosis, creating a greater burden for patients with complications.[15]

Digital Health Solutions in the form of blood glucose tracking Apps can be an answer to some of these issues and can shape the future of diabetes care in the country. One such tool is BeatO, which is committed to creating a digital health care ecosystem, and which can be accessed by all on their smart phones. It aims at increasing awareness and bringing behavioral changes by delivering personalized, actionable insights, reminders, caregiver alerts, diabetes educator support and guidance, educational content, doctor consultation and doorstep medicine delivery. As of today, it is already serving over 5 lakh diabetes patients across the country.[16] It has been instrumental in providing an ecosystem and delivering outcomes for the monitoring population and has been responsible for expanding the diabetes care landscape. Around 70% of its members are from tier 2 cities and beyond, 55% of members using this monitoring device are first-time glucometer users, and 83% of members have had their first interaction with a diabetes educator or coach on this platform. The depth and relevance of engagement have increased the time spent on the app—on average; a member spends approximately 10 minutes and 5 seconds daily on the platform.[16]

Affordability

Considering the high cost incurred at various steps of screening, diagnosis, monitoring and management, it is necessary to implement cost-effective measures for diabetes care. A systematic review on the costs of diabetes treatment in low- and middle-income countries reported that diabetes care is costly as many people have no health insurance and have to pay from their pocket.[17] In India, the average cost of outpatient diabetes care is about Rs. 11,000 per annum.[18] This poses a tremendous financial burden on the family, and there is a need to find ways to make diabetes care more affordable for the masses. Various studies have shown that low adherence to the medication is responsible for up to 50% of treatment failures, leading to complications. In the lower-income group, the cost of medication is a major reason for the poor adherence to antidiabetic medications.[19]

Digital technology that gives easy access to quality health care facilities will reduce the cost of diabetes care and improve patient outcomes. BeatO, for instance, has provided the right affordable tools (glucometer and strips) and free mobile application for the diabetes population, which has aided in lifting the financial burden by empowering the members to monitor more frequently in the last 5 years, thus driving better outcomes and lowering the cost for management over time.

Awareness

In a countrywide National NCD Monitoring Survey on Prevalence, Awareness, Treatment and Control of Diabetes in India, only 45.8% of patients were aware of their disease. Even among people who have been diagnosed with diabetes, only 40.6% were aware that diabetes could damage their vital organs. In another general population study, less than 30% of subjects knew about complications related to kidneys, eyes and nerves.[20]

Mobile health interventions help to improve diabetes risk behaviors and increase awareness about diabetes and its complications, etiology and manifestations. In the mDiabetes program implemented by Arogya World, there was an 11% increase in daily exercise, a 15% increase in the intake of 2 to 3 servings of fruits a day, and an 8% increase in 2 to 3 servings of vegetables per day by just text messages.[21]

RESOLUTION

To make India the Diabetes Care Capital of the World, we can take the help of the philosophy of Gandhi Ji's "Sarvodaya through Antyodaya", which means the development of all through the welfare of the weakest section of society.[22] A comprehensive, structured diabetes care program designed to provide holistic care to people living with diabetes will help ensure the democratization of diabetes care in India and beyond.

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■■■■

Dietary Pattern and Respiratory Diseases in Adults

MC GUPTA

Diet is regarded to be a potentially modifiable risk factor for impaired lung function.[1] Evidence suggests that a higher intake of antioxidants, especially vitamin C, may protect against impaired lung function and chronic obstructive pulmonary disease (COPD).[1]

DIETARY PATTERN AND FEV1 OR RESPIRATORY HEALTH

Prudent Dietary Pattern

A "prudent" dietary pattern (characterized by high consumption of fruit, vegetables, oily fish and wholemeal cereals, but by low consumption of white bread, added sugar, full-fat dairy products, chips and processed meat) is described to be strongly positively associated with lung function, particularly forced expiratory volume in 1 second (FEV1), in males and females, and negatively related to COPD in males.[1]

"Meat-dim Sum" Pattern

A "meat-dim sum" pattern (i.e., a diet rich in meats, sodium and refined carbohydrates) may increase the risk of developing cough with phlegm.[2]

Traditional Dietary Pattern

A traditional dietary pattern (characterized by higher intakes of red meat, processed meat, boiled vegetables, added fat, coffee, beer and potato and lower intakes of soy products, low-fat dairy products, tea, breakfast cereal, brown rice, pizza, juice and fruit) is said to be associated with a lower FEV1 and an increased prevalence of COPD.[3]

Cosmopolitan Diet

An increased intake of a cosmopolitan diet (characterized by higher intakes of vegetables, fish, chicken and wine and lower intakes of added fat, added sugar and potato) is reported to be associated with a small increased prevalence of wheeze and asthma.[3]

Mediterranean Diet

Children at age 6.5 years are less likely to have wheeze, atopic wheeze and atopy if their mothers had high compliance with a Mediterranean diet in pregnancy.[3]

Western Dietary Pattern

An increased intake of a Western dietary pattern (higher intakes of refined grains, cured and red meats, desserts and French fries) increases the risk of COPD and the frequency of asthma attacks among asthmatics (at least one attack/week).[3]

THE EFFECT OF NUTRIENTS OR FOODS IN LUNG FUNCTION

- **Sodium:** Dietary sodium has detrimental effects on asthma, airway hyperreactivity and symptoms of bronchitis.[2]
- **Refined foods:** A high intake of refined foods is associated with an accelerated longitudinal decline in FEV1 over 5 years and a small increase in a wheeze.[3]
- **Fast food and quick sugar:** A diet higher in fast food and quick sugar is associated with an increased prevalence of wheeze.[3]
- **Processed meat:** High consumption of processed meat (bacon, gammon, ham, corned beef, spam and luncheon meat, sausage and meat pies) is described to be associated with worse lung function and an increased risk of COPD.[4]
- **Alcohol:** Low-to-moderate alcohol consumption has been associated with improved lung function, while excessive intake has detrimental effects; however, the specific threshold remains undefined.[4]
- **Nonstarch polysaccharide:** Higher nonstarch polysaccharide intake reduces the risk of cough with phlegm and the symptoms of chronic bronchitis.[2]
- **Nuts and wine:** An increased intake of the nuts and wine pattern is associated with a significantly reduced risk of frequent asthma attacks.[3]

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- **Vitamin C:** A higher intake of vitamin C is associated with a lower rate of decline in FEV1.[3]
- **Apple:** Higher apple consumption is associated with a lower rate of decline; however, no significant association exists between intakes of individual nutrients and change in FEV1.[3]
- **Fruit and vegetables:** Fruit and vegetables intake is favorably associated with respiratory health due to the goodness of antioxidant vitamins (C, D, E and β-carotene), minerals (magnesium, calcium, selenium and potassium), dietary fiber and phytochemicals.[4]
- **Fresh fruit:** A reduction in fresh fruit consumption is associated with a higher rate of decline in FEV1 over 7 years.[3]
- **Omega-3 fatty acids:** Omega-3 fatty acids, primarily eicosapentaenoic acid (C20:5) and docosahexaenoic acid (C22:6), found in oily fish and seafood interfere with the body's inflammatory response and may destruct some of the inflammatory mechanisms involved in the physiopathology of COPD, asthma and obstructive lung disease.[4]

In Smokers without Respiratory Disease

- An alcohol-consumption pattern is associated with impaired lung function.[4]
- A Westernized pattern reduces lung function in women.[4]
- A Mediterranean-like pattern appears to be associated with preserved lung function.[4]
- Thus along with focusing on smoking cessation, dietary patterns must also be considered as they protect lung function.[4]

DIETARY PATTERNS AND LUNG CANCER

- Study on dietary patterns and lung cancer in men has shown a modest positive association for a dietary pattern characterized by pork, processed meat and potatoes.[2]
- A weak inverse association between dietary patterns and lung cancer has been described for dietary patterns focusing on vegetable intake.[2]

Knowledge of the beneficial or harmful effects of dietary patterns can be used in public health campaigns on a healthy lifestyle.[3]

TIPS FOR PRESCRIBING NUTRITIONAL SUPPLEMENTS TO YOUR PATIENTS

- Never use oral nutritional supplements (ONS) as first-line treatment.[5]
- Use the 'food first' approach initially, recommending the use of energy and protein-rich foods before prescribing ONS.[5]
- Initiate ONS prescribing when first-line dietary measures/'food first' approach has failed to achieve a positive change towards meeting goals after 1 month.[5]
- Review goals regularly and cease prescribing when goals are achieved. Consider possible interactions of ONS in warfarin-resistant patients.[5]
- Advise patients to take ONS between meals and not before meals or as a meal replacement to maximize their effectiveness and avoid spoiling appetite.[5]
- Prescribe ONS twice daily to be clinically effective and to ensure that calorie and protein intake is sufficient to achieve weight gain. If not food fortification should be used instead.[5]
- Give clear directions for use, e.g., "one to taken twice daily between meals" and not "As directed" as this has been shown to cause patients/carers to use the wrong dose.[5]
- Prescribe a 1-week prescription or starter pack initially to avoid wastage if products are not well accepted due to taste and palatability.[5]
- Avoid prescribing starter packs except for an initial trial, as they are usually more costly.[5]
- Issue monthly prescriptions on acute for 1 to 2 months after the patient has described his/her preferred flavor.[5]
- Avoid prescribing ONS in the repeat medications list without including a short review date to assess treatment goals.[5]
- Provide written information to the patient and/or carer regarding their ONS (supplement drinks) to inform them about their utility and time to stop. This will help manage the patient expectation of the duration of treatment.[5]

USE

- **Powdered shake - as first-line ONS:** Mix it with 200 mL full-fat milk as per manufacturers' instructions.[5]
- **Ready to drink liquid - as second-line ONS:** When a first-line powered ONS is not suitable or the patient is lactose intolerant or has difficulties preparing the powdered shake.[5]
- **Small volume 'compact' style ONS:** When the volume is a problem. It can be mixed with 100 mL of full-fat milk to make a 'compact' style ONS.[5]

- **Juice style drinks - as third-line ONS:** In patients who do not like or are unable to take milky drinks.[5]

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A New Technique to Remove Kidney Stones in Awake Patients

A new technique that combines two ultrasound technologies may provide a way to remove kidney stones from the ureter with little discomfort and without the need for anesthesia, according to a study published in the journal of *Urology*. The specialists assessed the novel technology to address the demand for a method to cure stones without surgery. The stones can then be moved and repositioned to facilitate passage using an ultrasound technique known as ultrasonic propulsion, or they can be broken up using a method known as burst wave lithotripsy (BWL). The study's objective was to evaluate the viability of breaking up stones in awake, nonanesthetized individuals using either BWL or ultrasonic propulsion. The study involved 29 patients. Thirteen patients had propulsion and burst wave lithotripsy, and 16 received propulsion alone. Stone movement occurred in 19 patients. After 2 weeks of follow-up, the results showed that 18 of 21 patients (86%) passed their stones, whose stones were found to be located in the ureter, closer to the bladder. The average time to stone passage in this group was almost 4 days. One patient felt immediate relief when the stone was dislodged from the ureter.

This is the first trial to examine the effects of BWL on shifting or dissolving stones in the ureter.

(*Source: https://m.dailyhunt.in/news/india/english/ani6791725081649696-epaper-anieng/ultrasound+can+move+break+up+kidney+stones+in+awake+patients+study-newsid-n430473908?listname=topicsList&index=23&topicIndex=7&mode=pwa&action=click*)

Impact of Social Disadvantages on the Brain Development of the Fetus

A new study published in the *Proceedings of the National Academy of Sciences* suggests new links between social disadvantages and fetal brain development. In the study, 399 mothers were oversampled for low-income and completed social background measures during pregnancy. Further, the researchers examined 289 brain development diffusion MRI scans of healthy newborns from socially diverse families shortly after birth.

The findings of the analysis revealed that prenatal exposure to measures of social disadvantages, such as education, insurance status, the income-to-needs ratio (INR), neighborhood deprivation and nutrition and psychosocial stressors like depression, stress, life events and racial discrimination, was associated with an altered microstructure of white matter in frontolimbic pathways of the brain. The frontolimbic pathways are the most important part of socio-emotional development. In the longitudinal study, mean diffusivity (MD) and fractional anisotropy (FA) were also measured via probabilistic tractography. The tractography revealed that social disadvantage was independently associated with lower mean diffusivity in the fetal brain. Also, similar results were observed after accounting for maternal medical morbidities and prenatal drug exposure.

(*Source: https://theprint.in/health/study-finds-impact-of-social-disadvantages-on-fetal-brain-development/1164047/*)

Any Advice which is Directive, Conclusive and is Likely to be Followed is Liable for Professional Negligence

A recent judgement of the Supreme Court in the state of Minnesota in the United States may have changed practice in the US. It has widened the scope under which a physician who has no patient-physician relationship might be sued for negligence.

On April 17, 2019, in **Warren v. Dinter,** the Court held that *"a physician-patient relationship is not a necessary element of a claim for professional negligence. A physician owes a duty of care to a third party when the physician acts in a professional capacity and* ***it is reasonably foreseeable that the third party will rely on the physician's acts and be harmed by a breach of the standard of care****."*

In this judgement, the Minnesota Supreme Court overturned the lower court rulings, stating in part that *"…To be sure, most medical malpractice cases involve an express physician-patient relationship. And a physician-patient relationship is a necessary element of malpractice claims in many states. But* ***we have never held that such a relationship is necessary to maintain a malpractice action under Minnesota law****…"*

The Court applied a foreseeability standard in their ruling… *"To the contrary:* ***when there is no express physician-patient relationship, we have turned to the traditional inquiry of whether a tort duty has been created by foreseeability of harm****…"*

The Facts

The patient, aged 54 years, sought medical care for abdominal pain, fever and chills, among other symptoms. She was evaluated by a nurse practitioner (NP). The test results showed very high white blood cell count, based on which the NP suspected that the patient had an infection and needed hospitalization. The NP placed a call to the local hospital to discuss admission with the admitting hospitalist. During this conversation, which lasted approximately 10 minutes and during which the admitting hospitalist was unable to view the patient's medical record, the decision was made by the hospitalist to not admit the patient. Her symptoms were attributed to her diabetes and outpatient follow-up was recommended. Three days later, the patient was found dead in her home. An autopsy concluded that the cause of death was sepsis caused by an untreated staph infection.

The patient's son brought a medical malpractice action against both the NP and the hospitalist. The trial court granted summary judgement to the defendants, and the Minnesota Court of Appeals affirmed the decision, holding there was no duty of care owed by the hospitalist because there was no physician-patient relationship. The hospitalist had only spoken to the NP by phone and had not seen the patient.

The following points were highlighted in the judgement:

- The NP did not have admitting privileges, and it was the hospitalist's sole duty to make decisions around patient admission.
- The hospitalist knew or should have known that the decision to admit or not would have been relied upon by the NP and her patient. The Court cited Skillings v. Allen (1919) and Molloy II (2004) and stated that *"Skillings and Molloy II teach us that* ***a duty arises between a physician and an identified third party when the physician provides medical advice and it is foreseeable that the third party will rely on that advice****."*
- The hospitalist knew or should have known that breach of the standard of care could result in harm. *"…It is a reasonable inference that Dinter must have known, or should have known, that a negligent decision not to admit Warren could harm her."*
- The Court referred to the hospitalist in this case as the "gatekeeper," distinguishing him from a "curbside consult" in that the hospitalist was the individual with the sole authority to make a decision around hospital admission. *"…Viewed in the light most favorable to Warren,* ***this interaction was neither a curbside consultation nor what Dinter and Fairview characterized as a 'professional courtesy'.*** *Simon did not know Dinter and, as the dissent notes, they had no pre-existing professional relationship. Unlike a curbside consultation, Simon did not contact Dinter to pick a colleague's brain about a diagnosis.*

In fact, she had already memorialized her own diagnosis in a letter to Warren's employer. Instead, Simon called Dinter pursuant to Fairview's protocol for hospital admissions. Consistent with that protocol, Fairview randomly assigned her to Dinter so that Fairview, through its gatekeeper, could make a medical decision on whether to accept and admit a new patient…"

Although this judgement was delivered by a US Court, this judgement highlights the fact that any advice which is directive, conclusive and/or confirms the decision and is likely to be followed is liable for professional negligence.

The Supreme Court of India too has held that telephonic consultations should be avoided as a routine.

In judgement in the matter of **Martin F. D'Souza vs. Mohd Ishfaq** (3541 of 2002) dated 17.02.2009 in the Supreme Court of India, the Bench of Justice Markandey Katju and GS Singhvi cited rules laid down by the Supreme Court in the Jacob Mathews case about precautions which doctor/hospitals/nursing homes should take to protect themselves from frivolous complaints of medical negligence.

They said, ***"No prescription should ordinarily be given without actual examination. The tendency to give prescription over the telephone, except in an acute emergency, should be avoided (54(b)."***

If needed, consultations on phone can be given, provided there is an established relationship between the doctor and the patient, i.e., the concerned patient is under the treatment of a doctor, and the doctor is aware of the nuances of the case. And most importantly, the doctor is fully cognizant of the attendant risks, both medical and medicolegal.

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In COVID Patients, a 50% Prevalence of Panic Disorder was Observed in a Study

In a study published in the *Asian Pacific Journal of Tropical Medicine*, it was shown that the measures taken for the containment of the COVID virus have led to the disruption of the physical and mental well-being of individuals. The study conducted by Amrita hospitals revealed a high prevalence of panic disorder with a cut-off score of eight on the Panic Disorder Severity Scale.

The study enrolled 109 COVID patients who were admitted to the hospital. Dr KP Lakshmi, Psychiatry and Behavior Medicine, stated that panic disorder was diagnosed in 54.3% of married patients, followed by 32% of unmarried and all widowed or widowed patients. She also added that the findings of the study showed that the prevalence of panic disorder was higher in patients with known physical illnesses and psychiatric illnesses. Similarly, the prevalence of panic disorder was lower in patients with recent alcohol use; however, it was increased in smokers. She explained that the decrease in panic disorder in patients with recent alcohol use was due to alcohol acting as a central nervous system depressant, while, on the other hand, she explained that tobacco is a central nervous system stimulant. Hence, the increased prevalence of panic disorders among smokers.

(*Source: https://www.daijiworld.com/news/newsDisplay?newsID=1008685*)

After COVID Infection, Patients Suffer from At Least 1 Out of 3 COVID Symptoms

A study published in the *JAMA Network* showed that 6.2% of 1.2 million people experienced at least one of the three long COVID symptoms, namely persistent fatigue with bodily pain or mood swings, cognitive problems or ongoing respiratory problems after 3 months of acute infection onset. In the meta-analysis study, 54 studies were taken for analysis, out of which 44 were published studies and 10 were collaborating cohort trials.

The study revealed that 15.1% of the patients continued to experience long COVID symptoms for more than 12 months. The study also revealed that the risk of long-term COVID was greater in female patients in comparison to their male counterparts. Similarly, the risk of long COVID symptoms was also found to be greatest in those who needed hospitalization for the initial SARS-CoV-2 infection, particularly among those needing intensive care unit care. The findings of the study revealed that one of the three self-reported long COVID symptom clusters included 3.7% for ongoing respiratory problems, 3.2% for persistent fatigue with bodily pain or mood swings and 2.2% for cognitive problems after adjusting for health status before COVID.

(*Source: https://www.daijiworld.com/news/newsDisplay?newsID=1008847*)

HCFI Dr KK Aggarwal Research Fund

Coronavirus Updates

WHO report terms anxiety and burnout among healthcare workers as a "pandemic within a pandemic"

A new report prepared jointly by the Qatar Foundation, World Innovation Summit for Health (WISH) and the World Health Organization (WHO) has highlighted the high levels of anxiety, depression and burnout among health and care workers during the pandemic. Anxiety symptoms were reported by 23% to 46%, while 20% to 37% faced symptoms of depression. Almost half (41-52%) of them experienced burnout. Jim Campbell, WHO Director of Health Workforce said, "Well into the third year of the coronavirus disease 2019 (COVID-19) pandemic, this report confirms that the levels of anxiety, stress and depression among health and care workers has become a "pandemic within a pandemic"... (*Source: WHO, Oct. 5, 2022*)

France experiencing the eight wave of coronavirus

France is in the midst of the eight wave of coronavirus. As per data published earlier this week, the 7-day moving average of daily new cases was recorded to be 45,631, which is the highest since early August. The total number of hospitalizations has also increased to 15,166 as has the number of intensive care unit (ICU) COVID patients at 843… (*Source: Medscape, Oct. 5, 2022*)

Rising prevalence of BA.4.6 in the US

The BA.4.6 sublineage of the Omicron variant of concern has been steadily rising in the United States and now makes up around 13% of the circulating severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants in the United States compared to 11.9% in the preceding week, as per data from the Centers for Disease Control and Prevention (CDC). The BA.5 continues to be the dominant strain and accounts for 81.3% cases, while the BA.4 is responsible for just 1.1% of cases… (*Source: Reuters, Oct. 5, 2022*)

Impact of masks on communication for the deaf people

Majority of the deaf and hard of hearing people found it difficult to communicate during the pandemic. Nearly 60% reported feeling "disconnected from society", while 76% reported missing important information. Those with late-onset and "severe or profound" deafness faced challenges while communicating. People who relied on sign language thought that they were more disconnected because they missed reading the signs… (*Source: Cognitive Research: Principles and Implications, Sept. 5, 2022*)

Norwegian Cruise Line relaxes mandatory testing and masking rules

In a far cry from the days when the Diamond Princess Cruise became the hotspot of COVID-19, the Norwegian Cruise Line has relaxed the necessity of testing, masking and vaccination for its passengers. However, all travel guidelines as required in the country of visit would still be observed stated the cruise line… (*Source: Medscape, Oct. 4, 2022*)

New BF.7 and BA.5.1.7 Omicron sublineages detected in China

Two new sublineages of the Omicron variant have been detected in China. BF.7 and BA.5.1.7 are highly contagious in nature, which makes them highly transmissible. The BF.7 is a subvariant of the BA.5.2.1… (*Source: ETHealthworld, Oct. 13, 2022*)

XBB: A new recombinant variant of SARS-CoV-2

A new recombinant variant "XBB" has emerged as a significantly more immunoevasive strain of SARS-CoV-2. It is a combination of BJ.1 and BA.2.75, which are sublineages of the Omicron variant. In a bioRxiv preprint study, it has shown the strongest resistance to monoclonal antibodies. It was first isolated in Singapore and has been detected in Bangladesh, Denmark, Japan, Australia and the US. Almost half of the new cases are due to this new recombinant variant. So far, 71 cases have been detected in India from Maharashtra, Odisha, West Bengal and Tamil Nadu… (*Source: First Post, Oct. 14, 2022*)

Drug interactions between Paxlovid and drugs for heart disease

A review paper published in the *Journal of the American College of Cardiology* has cautioned about potential drug-drug interactions between nirmatrelvir-ritonavir (Paxlovid) and other commonly used cardiovascular drugs such as antiarrhythmics, antiplatelets and anticoagulants, statins like simvastatin or lovastatin,

ranolazine and immunosuppressive agents… (*Source: ACC, Oct. 12, 2022*)

US FDA grants EUA to bivalent booster vaccines for use in young children

The US Food and Drug Administration (FDA) has granted emergency use authorization (EUA) to Moderna and Pfizer bivalent booster vaccines to be administered as a single dose in young children. Moderna's bivalent vaccine has been approved for use in children aged 6 years and older, while the updated Pfizer vaccine can now be given to children aged 5 years and older… (*Source: US FDA, Oct. 12 2022*)

IndoVac: Indonesia's first indigenous COVID-19 vaccine

Indonesia will soon start manufacturing its first indigenous COVID-19 vaccine "IndoVac". The vaccine is being developed in collaboration with Baylor College of Medicine in Texas, USA. Less than 75% of the eligible population has completed their two-dose primary vaccination; 27% have taken one booster dose, while less than 1% have taken the second booster dose… (*Source: Medscape, Oct. 13, 2022*)

COVID-19 rearing up again in Europe

Europe may be looking at a new wave of COVID-19 as cases across Europe region are showing a rising trend, according to the WHO and European Centre for Disease Prevention and Control (ECDC). In the Week ending 2nd October, only the European Region recorded an increase of 8% in new weekly cases, according to WHO's weekly Epidemiological Update dated 5th October. "With the arrival of autumn and winter, the resurgence of influenza can also be expected", according to a press release. The uptake of vaccine has not been very optimistic in Europe… (*Source: WHO, Oct. 12, 2022*)

"COVID-19 remains a public health emergency of international concern", says WHO

The Emergency Committee of WHO on COVID-19 has cautioned that "COVID-19 remains a public health emergency of international concern". The Committee urged countries to update their pandemic "preparedness and response plans".

Testing and treatment facilities, including vaccination should be accessible to all, especially those at high-risk of getting the infection. At a media briefing on 12th October, the WHO Director General Dr Tedros Ghebreyesus said, "This pandemic has surprised us before and very well could again"… (*Source: WHO, Oct. 19, 2022*)

CDC to include COVID-19 vaccine in the routine vaccination schedule

The CDC will update the 2023 annual immunization schedules for both children and adults by including COVID-19 vaccines as recommended by the CDC's Advisory Committee on Immunization Practices (ACIP). The updated vaccination schedule will be published early next year… (*Source: CDC, Oct. 20, 2022*)

Europe's drug regulatory agency recommends Moderna's bivalent vaccine as booster

Moderna's bivalent COVID-19 booster vaccination will soon be available in Europe for persons aged 12 years and above following the European Medicines Agency (EMA)'s recommendation for authorization. EMA has also granted authorization to Moderna and Pfizer-BioNTech vaccines for children as young as 6 months… (*Source: Reuters, Oct. 20, 2022*)

Novavax COVID-19 vaccine now also authorized as booster

The Novavax COVID-19 vaccine is now also available as a booster dose in the United States. Earlier this week, the US FDA authorized the vaccine as booster for adults who cannot get the updated boosters or those who do not want to take any other booster dose… (*Source: Medscape, Oct. 20, 2022*)

No pre-departure COVID test required for travelers to Qatar

Football fans traveling to Qatar for the World Cup will no longer be required to have a negative pre-departure COVID-19 test. Earlier, a negative COVID-19 test was necessary for all the inbound travelers regardless of their vaccination status. The Health Ministry has also done away with the need for showing the COVID status on a contact tracing App prior to entering the stadium or other public places. Citizens will also not be asked to get themselves tested within 24 hours of returning home after travel abroad… (*Source: Reuters, Oct. 26, 2022*)

Report predicts a slow rise in COVID cases globally

A report from the University of Washington's Institute for Health Metrics and Evaluation (IHME) has estimated that the number of daily cases would increase to 18.7 million by February next year from the present 16.7 million average daily cases. "It forecast that global daily deaths would average 2,748 people on February 1, compared with around 1,660 currently." This rise in cases is likely to be propelled by the oncoming winter season. However, a surge in deaths is not likely to occur… (*Source: Medscape, Oct. 26, 2022*)

Wuhan goes under partial lockdown

Wuhan, the epicenter of the pandemic, has locked one of its districts following a spurt in COVID-19 cases in view of the zero-COVID policy still being followed in China. Nearly 1 lakh residents have been asked to stay at home from Wednesday (Oct. 26) to Sunday (Oct. 30). Outpatient services have been put on hold in the Union Hospital in Wuhan. Online teaching has resumed in universities in Wuhan… (*Source: Medscape, Oct. 26, 2022*)

The first inhalable vaccine against COVID-19?

As per media reports, Shanghai residents are being administered an inhalable vaccine against COVID-19 as booster dose for people who have completed their primary vaccination. The vaccine developed by CanSino Biologics is an aerosolized form of its adenovirus vaccine. The vaccine is in the form of a mist, which is slowly inhaled into the mouth through a nozzle. The vaccinated person is required to hold the breath for 5 seconds… (*Source: Indian Express, Oct. 27, 2022*)

Gout increases risk of COVID hospitalization and mortality

Gout patients with COVID-19 are at greater risk of acquiring COVID-19 and experience serious adverse outcomes, including hospitalization and death, despite having completed their vaccination schedule compared to people without gout. Women with gout were 1.5 times more likely to be admitted to hospital for their illness and nearly 2.5 times more likely to die due to the illness… (*Source: Arthritis Rheumatology, Sept. 9, 2022*)

Weekly new COVID-19 cases continue to decline globally

A decrease of 17% was noted in the weekly COVID-19 cases in the last week of October compared to the preceding week, with more than 2.3 million new cases, as per the WHO's latest COVID-19 Weekly Epidemiological Update although the Americas and the Western Pacific Region have shown a slight uptick in cases. A decrease in testing may preclude accurate estimation of the new cases, cautions the WHO… (*Source: WHO, Nov. 2, 2022*)

Pfizer starts phase 1 trial of a COVID-flu combination vaccine

Pfizer-BioNTech will soon start testing of its mRNA-based combined coronavirus and influenza vaccine in the United States. The phase 1 trial will begin with 180 volunteers…(*Source: Reuters, Nov. 3, 2022*)

COVID-19 and gut dysbiosis

COVID-19 is significantly associated with gut microbiome dysbiosis, states a study reported in Nature Communications. This predisposes patients to secondary blood stream infections, which may be potentially life-threatening similar to that seen among immunocompromised patients such as those with cancer…(*Source: Nature Communications, Nov. 1, 2022*).

A 50-folds increase in ventilation rates lowers risk of infection with Omicron

To keep the likelihood of infection <1% with the Alpha SARS-CoV-2 variant, the required ventilation rates are 650-1,200 m^3/hour for exposure time of 15 minutes and 8,000-14,000 m^3/hour for 3 hours of exposure. For Delta variant, the rates increased to 2,200-6,800 m^3/hour for 15 minutes, and 26,000-80,000 m^3/hour for 3 hours. For Omicron variant, the ventilation rate increased 50-folds to 5,400-17,000 m^3/hour for 15 minutes and 64,000-2,50,000 m^3/hour for 3 hours. However, wearing N95 masks would reduce this requirement…(*Source: Building Simulation, Oct. 19, 2022)*

Include heavy menstrual bleeding as a possible side effect of mRNA vaccines, says EMA

The Pharmacovigilance Risk Assessment Committee (PRAC) of the EMA has recommended updating of the label for the Moderna and Pfizer mRNA vaccines by including heavy menstrual bleeding as a side effect. According to the committee, "there is at least a reasonable possibility that the occurrence of heavy menstrual bleeding is causally associated with these vaccines". The bleeding has been "non-serious and temporary"…(*Source: EMA, Oct. 28, 2022*)

With inputs from Dr Monica Vasudev

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AIOC 2022: 80th Annual Conference of All India Ophthalmological Society

CI-DME: ALGORITHMS

Dr Rajiv Raman, Chennai

The guiding principles of treatment of center-involving diabetic macular edema (CI-DME) include:

- Switch anti-VEGF (vascular endothelial growth factor)/switch to laser or steroids in nonresponders. Optical coherence tomography (OCT) and vision are key tests for determining initial treatment choice and follow-up.
- Vitrectomy has a role in cases of vitreomacular traction and select cases of nonresponding DME.
- Classify DME as center involving and center not involving.
- Glycemic control and control of blood pressure (BP), lipids, anemia are crucial.
- Anti-VEGFs are the first-line of treatment for center involving DME.

COMPLEX TRACTIONAL RETINAL DETACHMENTS: DIABETIC AND VASCULITIS

Dr Vishali Gupta, Chandigarh

- Preoperative considerations include good metabolic control, preoperative anti-VEGF agents to reduce intraoperative bleed and preoperative pan-retinal photocoagulation (PRP) in diabetic patients to maintain a safe distance from the base of fibrous membrane. It is important to identify the right plane of dissection.
- Use a cutter that allows working very close to the retina (bevelled, 10,000 cr/min).
- Identify vitreoschisis even though you may feel that vitreous dissection seems apparently complete.

TRAUMATIC SUBLUXATION WITH OR WITHOUT VITREOUS IN AC: WHEN AND HOW TO INTERVENE?

Dr Siddhartha Ghosh, Kolkata

- Ectopia lentis is displacement or malposition of the crystalline lens of the eye. Most commonly it occurs due to trauma, but can also occur due to ocular and systemic diseases.
- Intervention is required when vision or integrity is affected.
- How to intervene? Need to tackle vitreous first, need to preserve capsular bag as far as possible, judicious implantation of intraocular lens (IOL).

SELECTIVE ENDOTHELIALECTOMY IN PETERS' ANOMALY: LONG-TERM CLINICAL OUTCOMES IN 34 EYES OF 24 CHILDREN

Dr Muralidhar Ramappa, Hyderabad

- Peters' anomaly is the most common anterior segment developmental abnormality and presents with a central or paracentral corneal opacification. It accounts for nearly half of all children born with corneal opacities and is bilateral in 60% to 80%.
- Management of these children involves pharmacological pupillary dilatation, optical iridectomy, rotational corneal autograft, endocapsular cataract extraction, penetrating keratoplasty.
- A retrospective consecutive interventional case series was conducted at LV Prasad Eye Institute in Hyderabad between 2012 and 2020. This study validates the outcomes of Selective Endothelialectomy in Peters' Anomaly (SEPA), a novel and less invasive surgical strategy for the treatment of Peters' anomaly. A significant regression of opacity was seen in 85% with marked improvement in functional vision. This study demonstrated for the first time that SEPA can be used even in cases of keratolenticular adhesion as long as the opacity is not >7 mm or at least half of the peripheral cornea is clear.
- SEPA results are extremely promising and can be an effective surgical alternative to full-thickness penetrating keratoplasty benefiting hundreds of children with Peters' anomaly related blindness worldwide.

ACQUIRED VITELLIFORM LESIONS

Dr Deeksha Katoch, Chandigarh

- Vitelliform lesions can be hereditary or acquired. Hereditary lesions include Best's vitelliform

dystrophy, adult-onset foveomacular vitelliform dystrophy and pattern dystrophy.

- Acquired vitelliform lesions (AVLs) occur in a variety of different clinical entities such as age-related macular degeneration (AMD), central serous choroidopathy or tractional maculopathies. The natural course is biphasic with a period of growth followed by resorption.
- Most patients retain reading vision in at least one eye throughout their lives.
- They share common OCT, fluorescein angiography and fundus autofluorescence (FAF) features regardless of the underlying clinical diagnosis.
- The diagnosis of choroidal neovascularization in the setting of AVLs using fluorescein angiography alone can be challenging.
- Integration of multimodal imaging (OCT, FAF, OCT-A) can help resolve dilemmas in most cases. This can help refine management and avoid unnecessary interventions and follow-ups in such patients.

PROLIFERATIVE DIABETIC RETINOPATHY: MANAGEMENT APPROACH

Dr Pramod S Bhende, Chennai

- Proliferative diabetic retinopathy (PDR) is a proliferative vascular retinopathy seen in diabetics.
- Ocular investigations include wide field fundus photo, fundus fluorescein angiography (FFA)/ widefield FFA, OCT/OCTA, USG B scan. The systemic investigations include fasting blood sugar, postprandial blood sugar, A1c, hemoglobin, lipid profile and BP.
- PDR with DME with no macula-threatening traction, recurrence of neovascularization after a good PRP and partial vitreous hemorrhage preventing completion of PRP with no visible traction are ideal candidates where anti-VEGF may have a role.
- Laser PRP is still a mainstay of treatment for PDR.
- Anti-VEGF can be combined with PRP in eyes with CI-DME and recurrent neovascularization.
- Role of anti-VEGF as monotherapy is still debatable but in advanced diabetic eye, presurgery intravitreal anti-VEGF helps to minimize intraoperative bleeding for more complete removal of fibrovascular proliferation.
- Tractional retinal detachment/Combined retinal detachment are the commonest indications for vitrectomy in PDR.
- Early treatment and good metabolic control give better final outcome. Long-term regular follow-up is essential in these patients.

CSR AND CME

Dr Raju S, Bengaluru

- Central serous retinopathy (CSR) is considered the fourth most common nonsurgical retinopathy associated with fluid leakage.
- Cystoid macular edema (CME) is the most common complication post-cataract surgery.
- Risk factors for CSR include stress, smoking, gastroesophageal reflux disease (GERD), type A personality, hypertension, drugs like corticosteroids, phosphodiesterase-5 inhibitors (sildenafil, tadalafil).
- History can provide clues. A typical CSR case is characterized by middle-age, males, sudden-onset painless, micropsia, positive scotoma, hyperopic glasses, decrease in vision/distortion/central scotoma. Features of CME include painless/slight pain/discomfort, photophobia, previous episodes of history of redness.
- Clinical findings in CME are blunted or irregular foveal light reflex, retinal thickening and/or intraretinal cysts in the foveal region.
- Clinical findings in CSR are neurosensory retinal detachment, pigment epithelial detachment, retinal pigment epithelium mottling and atrophy and subretinal fibrin. Rarely, subretinal lipid or lipofuscinoid flecks also may be seen.
- Early CME is developing <4 months of surgery, late CME is >4 months of surgery, chronic CME persists for >6 months with visual impairment.
- Clinical CME is detectable visual impairment, angiographic and/or biomicroscopic findings. Clinical diagnosis is confirmed by OCT and fluorescein angiography.
- There is no robust support for the use of anti-VEGF treatments in CME. Reserved only for eyes unresponsive to conventional treatment modalities.
- In edema due to infections where immunosuppressive therapy could be detrimental to the resolution of infection, anti-VEGF may have a role.

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News and Views

Phage Therapy for Cystic Fibrosis

An trial supported by National Institute of Health's National Institute of Allergy and Infectious Diseases to investigate the safety and efficacy of an experimental phage therapy "WRAIR-PAM-CF1" against chronic *Pseudomonas aeruginosa* infection in the airways of adults with cystic fibrosis (CF) has started in the United States. The phase 1b multicenter trial conducted by the Antibacterial Resistance Leadership Group (ARLG) will recruit up to 72 patients with CF from across the country.

According to an NIH press release, the components of WRAIR-PAM-CF1 include "a cocktail of four bacteriophage species that naturally infect *P. aeruginosa* and take over its cellular processes, killing the bacterium in the process. The phages in the cocktail are highly specific and do not attack human cells". The press release further states that these phages do not carry harmful genes such as those pertaining to antibiotic resistance, which could inadvertently be transferred to the bacteria they infect.

Three doses of the anti-pseudomonal phage therapy would be tested. One of the three doses would be administered to each participant as a single IV infusion. To begin with, in stage 1 of the trial, the three doses would be tested on two participants for each dose followed by close monitoring of the volunteers for 4 days. A preliminary analysis will be carried out to determine the dose. Up to 50 participants would be enrolled for stage 2 of the trial if there are no significant severe safety concerns in stage 1. The study subjects would then be randomized to receive either the selected dose of the experimental therapy or a placebo. They would be regularly screened on follow-up visits.

Will phage therapy circumvent the escalating crisis of antibiotic resistance? Only time will tell.

(*Source: NIH Press Release, October 4, 2022. Available at: https://www.nih.gov/news-events/news-releases/nih-supported-clinical-trial-phage-therapy-cystic-fibrosis-begins*)

A Vaccine to Protect Newborns from Whooping Cough

A vaccine to protect newborns from pertussis (whooping cough), has been approved by the US Food and Drug Administration (FDA).

The Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine, Adsorbed (Tdap) is the first vaccine, which can now be given to pregnant mothers during the third trimester of pregnancy to prevent whooping cough in infants younger than 2 months of age. Administration of the vaccine during pregnancy enhances antibody levels in the mother, which are transferred to her baby. The vaccine has shown 78% efficacy in preventing whooping cough in infants less than 2 months of age.

"Infants younger than 2 months of age are too young to be protected by the childhood pertussis vaccine series", said Peter Marks, MD, PhD, Director of the FDA's Center for Biologics Evaluation and Research.

The vaccine is administered in a single dose of 0.5 mL.

The most commonly reported adverse effects in clinical trials have been local pain and redness at the site of injection. Headache, fatigue and gastrointestinal symptoms have also been reported. No vaccine-related maternal or fetal/newborn side effects have been observed with the vaccine, as per the FDA.

(*Source: US FDA News Release, October 7, 2022*)

Decline in the Levels of Amyloid Beta Protein Leads to Alzheimer's Disease

In a study published in the *Journal of Alzheimer's Disease*, researchers revealed that Alzheimer's disease is caused by a decline in levels of a protein called amyloid-beta. In the study, they hypothesized that plaques are simply a consequence of the decreased levels of soluble amyloid-beta in the brain. These levels decrease because the normal protein, under situations of biological, metabolic or infectious stress, transforms into abnormal amyloid plaques.

In the study, the researchers analyzed the levels of amyloid-beta in a subset of patients with mutations that indicate overexpression of amyloid plaques in the brain, which is thought to increase the risk of the likelihood of developing Alzheimer's disease.

The researchers found that with a baseline level of soluble amyloid-beta in the brain above 270 pg/mL, people can remain cognitively normal regardless of the number of amyloid plaques in their brains. In comparison to the control, they found a similar pattern

in patients who were thought to have the highest risk of Alzheimer's disease.

The findings of the study also revealed that individuals already accumulating plaques in their brains who can generate high levels of soluble amyloid-beta have a lower risk of evolving into dementia.

(*Source: https://theprint.in/health/research-reveals-that-alzheimers-disease-is-caused-by-decline-in-levels-of-amyloid-beta/1155245/*)

More Than 60 New Genetic Regions that may Cause Stoke has been Identified

The study published in the *Nature Journal* revealed 61 new genetic regions associated with stroke that are potential drug targets to prevent or treat the second leading cause of death worldwide. In the study, data from 2.5 million people from five different ancestries, more than 2,00,000 of whom had a stroke, was analyzed by the members of the GIGASTROKE consortium.

The consortium included Professor Dr Kameshwar Prasad, Former Head of the Department of Neurology at the All India Institute of Medical Sciences (AIIMS), Delhi, who stated that the population studied in the research has a fairly global representation, including South Asia, which includes India and Pakistan, Africa, East Asia, Europe and Latin America. He further added that the combined results from different ancestries and regions made things clearer at a micro level.

The study included 1,10,182 patients who had a stroke and 1,503,898 participants as control individuals. Based on the participant data, the team identified association signals for stroke and its subtypes at 89 (61 new) independent gene loci. During a follow-up including 89,084 additional cases of stroke and 1,013,843 control individuals, it was seen that 87% of the primary stroke risk regions and 60% of the secondary stroke risk regions were replicated.

The findings of the study highlighted the F11, KLKB1, PROC, GP1BA, LAMC2 and VCAM1 regions as possible targets, with drugs already under investigation for stroke in the F11 and PROC regions. They also found that the frequency of a genetic region called COBL was higher in people suffering from neurological disorders in India and Pakistan, while no such frequency of this region was identified in patients from other ancestries.

(*Source: https://www.tribuneindia.com/news/health/over-60-new-genetic-regions-behind-stroke-identified-may-lead-to-new-therapies-438097*)

High Levels of Stress were Flagged in the Age Group of 31 to 40 Years in a Survey

Healthians, a diagnostics company, surveyed over 250 Indian cities. The survey revealed that 6 in every 10 Indians had abnormal levels of bad cholesterol, with the highest prevalence among the 31- to 40-year age group. The survey conducted by the firm anonymized the data collected from 2.66 million people in the age group of 20 years and older and revealed that 63% had high low-density lipoprotein (LDL) cholesterol levels in their blood.

Mr Deepak Sahni, Founder and CEO of Healthians, stated that in the 31- to 40-year group, 69% of the patients tested had abnormal levels of LDL. He added that this could be an indication of high-stress levels in that age group.

This, according to doctors, is the cause of the recent increase in cardiac arrests. She added that, as per the survey, 3 in every 10 Indians have abnormal levels of total cholesterol in their bloodstream, with the highest prevalence amongst the 31 to 40 age group.

The survey results also showed that 36% of Indians in the 40 to 60 age range have abnormal levels of total cholesterol. Interestingly, those who are older had lower levels of total cholesterol. The corresponding percentage was 30% in the 60 to 70 age group, while it was 24% in the 70 to 80 age group.

When the data were analyzed based on the gender criteria, it was found that males had a higher prevalence of abnormal levels of LDL, triglycerides and total cholesterol. About 64% of the males tested had abnormal LDL, 47% had abnormal triglycerides and 32% had abnormal total cholesterol compared to 63%, 30% and 29% in females, respectively. However, more females had abnormal high-density lipoprotein (HDL) levels compared to males.

(*Source: https://www.thehindu.com/sci-tech/health/diagnostics-firm-healthians-flags-high-stress-level-in-31-40-age-group/article65967463.ece*)

Blueprint for Research Released by WHO on Dementia, Dubbed as the 7th Leading Cause of Death

Recently, the World Health Organization (WHO) announced the development of a blueprint for dementia research, a first-of-its-kind initiative for non-communicable diseases. In a statement, the WHO noted that the blueprint has been designed to guide policymakers, funders and the research community on

dementia research. The blueprint will make decision-making and research more efficient, equitable and impactful.

Dementia is one of the greatest health challenges of our generation, dubbed as the 7th leading cause of death globally. However, dementia research accounts for <1.5% of total health research output. According to WHO, strategies are needed for better understanding, preventing and treating the underlying diseases that cause dementia and, at the same time, providing care and support for people with dementia. Moreover, dementia research needs to be conducted within an enabling environment where collaborations are fostered and equitable and sustained investment is realized.

The blueprint for dementia research is built on lessons learned from WHO efforts to prioritize research and coordinate research activities for infectious diseases, such as considering the entire dementia research spectrum, incorporating diagnostics and therapeutics, as well as emerging scientific and technological advances such as artificial intelligence, multi-omics and biomarkers, and also encompassing epidemiology, health economics, care and carer research, risk reduction, and brain health across the life course. The blueprint also provides insight into different drivers of research, such as sustainable funding, diversity and equity, and the involvement of people with lived experience of dementia throughout the research development process.

(*Source: https://health.economictimes.indiatimes.com/news/industry/dementia-who-gives-blueprint-for-research-on-7th-leading-cause-of-death/94656644*)

Smartphone-linked Artificial Pancreases Developed by IISc to Monitor Blood Sugar Level

A research team from IISc, Bengaluru, in collaboration with doctors from MS Ramaiah Medical College, has developed an artificial pancreas system. This can monitor and control blood sugar levels in real-time to help people with type 1 diabetes who need to take insulin regularly to avoid low blood sugar (hypoglycemia) or high blood sugar (hyperglycemia).

The Artificial Pancreas (AP) setup developed by Dr Radha Kant Padhi, Professor in the Department of Aerospace Engineering and Robert Bosch Centre for Cyber-Physical Systems, mimics the body's closed loop system that regulates insulin production. The setup has three parts, namely a sensor, an insulin pump and an Android app.

The sensor is a small coin-like device with a tiny needle-like extension that is stuck to the skin like a patch or band-aid that will monitor the glucose concentration in the subcutaneous tissue continuously. The sensor is connected to an insulin pump that will infuse insulin under the skin. The pump is a small rectangular device that can be carried around in a pocket. Both the sensor and the pump are connected to the android app. The app analyses the data sent by the sensor and determines how much insulin should be pumped into the body through the insulin pump. The key component of the app is the Model Predictive Control (MPC). This predicts how much insulin is required based on the sensor's data and sends the signal to the insulin pump. This predictive nature makes MPC a good algorithm for the AP system since blood glucose levels of type 1 patients need to be continuously regulated.

(*Source: https://health.economictimes.indiatimes.com/news/medical-devices/bengaluru-iisc-develops-smartphone-linked-artificial-pancreas-to-monitor-blood-sugar-levels/94673859*)

In India, Vedanta's Medical Arm Ties Up with Anuva for Cancer Research

Recently, Vedanta's BALCO Medical Centre (BMC), one of India's leading cancer hospitals, announced a strategic collaboration with Anuva, a genomics biotech company, to build a Cancer Genomics Biobank for cancer research in India. The companies aim to use this cancer bio/data bank to identify and develop precision medicine for cancer treatment in India.

Dr Jyoti Agarwal, Chairperson of BALCO Medical Centre, stated that the collaboration with Anuva will bring together the best of knowledge, technology and research to serve the people of India better through precision medicine and targeted treatment.

She continued by saying that this cancer-specific bio/data library will speed up research initiatives by fusing biological characteristics with known risk factors to identify the key genes that drive cancer progression. The resulting knowledge will improve the understanding of how genetic variants influence cancer, thereby increasing the effectiveness of diagnosis and treatment.

(*Source: https://www.tribuneindia.com/news/health/vedantas-medical-arm-ties-up-with-anuva-for-cancer-research-in-india-438735*)

Risk of Dementia is Increased by 2.5 Times Due to Schizophrenia

A new systematic review and meta-analysis published in *Psychological Medicine* reveal that psychotic disorders have a strong link with dementia in comparison to other mental health disorders, such as depression or

anxiety. The study showed that people with psychotic illnesses such as schizophrenia are 2.5 times more likely to develop dementia than those who do not have a psychotic disorder.

In the study, the researchers analyzed the data from 11 studies from nine countries in four continents, which included almost 13 million participants in total. After analysis, they found that due to various psychotic illnesses, there was a greater risk of dementia in later parts of life, independent of the age at which someone first experienced their mental illness. Additionally, they discovered that individuals with a history of psychotic diseases are significantly more likely to receive a dementia diagnosis while they are still in their 60s than the general population. The findings of the study add to the list of modifiable risk factors for dementia. One such modifiable risk factor is post-traumatic stress disorder (PTSD), which can increase the likelihood of dementia along with other factors such as depression and anxiety. The author of the article stated that people with psychotic disorders are more likely to have other health conditions such as cardiovascular disease (CVD) or obesity, which can increase the risk of dementia. She added that they are also more likely to have a poor diet, smoke or use drugs, which may harm their health in ways that could increase their likelihood of developing dementia.

(*Source: https://www.hindustantimes.com/lifestyle/health/schizophrenia-might-enhance-dementia-risk-2-5-times-study-101665112009172.html*)

Risk of Obesity in Kids is Increased by the Intake of Ultra-Processed Food by Mothers

A recent study published in the *BMJ* revealed that a mother's use of ultra-processed foods was connected to an elevated risk of being overweight or obese in her kids, regardless of other lifestyle risk factors. According to the WHO, 39 million children were overweight or obese in 2020, leading to increased risks of heart disease, diabetes, cancer and early death.

The study suggested that mothers may benefit from limiting their intake of ultra-processed foods. The researchers also suggested that the dietary guidelines should be refined, including the removal of financial and social barriers to improve nutrition for women of childbearing age and to reduce childhood obesity. In the study, the researchers used data from the Nurses' Health Study II (NHS II) and the Growing Up Today Study (GUTS) I and II. The researchers also considered a range of other potentially influential factors, such as the mother's weight (body mass index [BMI]), physical activity, smoking, living status and partner's education, as well as children's ultra-processed food consumption, physical activity and sedentary time.

Based on the analysis, the study results showed that a mother's ultra-processed food consumption was associated with an increased risk of obesity or being overweight in her offspring. For example, a 26% higher risk was seen in the group with the highest maternal ultra-processed food consumption (12.1 servings/day) in comparison to the lowest consumption group (3.4 servings/day). It also found that prenatal ultra-processed food intake had no significant association with an increased risk of offspring being overweight or obese.

(*Source: https://theprint.in/features/study-mothers-intake-of-ultra-processed-food-associated-with-risk-of-obesity-in-kids/1156511/*)

New 3D Technique Developed to Treat Diabetic Foot Ulcers

Researchers at Queen's University Belfast have created a new cost-effective bandage therapy called a scaffold to treat diabetic foot ulcers, which provides better patient outcomes.

The scaffolds, which are created by 3D bioprinting, gradually release antibiotics over a 4-week period to cure the wound. The study was published in *The Journal of Drug Delivery and Translational Research*.

The scaffold structure, according to experts, is a unique carrier for cell and medication transport that improves wound healing. By using these scaffolds, which function like windows, surgeons can continuously monitor the healing process without having to remove them, as frequent interference for changing the dressing increases the risk of infection and slows down the healing process. "The 'frame' contains an antibiotic that kills the bacterial infection, and the 'glass', is made of collagen and sodium alginate, which might include a growth factor that promotes cell growth. The scaffold has two molecular levels, each of which is crucial to the healing of the wound."

This new development has been shown to enhance the quality of life among patients and decrease the cost of treatment and also the clinical burden in diabetic foot ulcer treatment.

(*Source: https://m.dailyhunt.in/news/india/english/ani67917250816496966-epaper-anieng/new+3d+technique+developed+by+researchers+to+revolutionise+diabetes+treatment-newsid-n429702646?listname=topicsList&topic=health%20fitness&index=2&topicIndex=8&mode=pwa&action=click*)

Risk of Adverse Outcomes Increased by Long-term Antidepressant Use

Long-term antidepressant usage has been associated with an increased risk of adverse effects, including CVD, cerebrovascular disease (CV), coronary heart disease (CHD) and all-cause mortality, according to a study published in the *British Journal of Psychiatry Open*.

The study involved 2,22,121 participants whose information was connected to primary care records in 2018. They found that 10-year antidepressant usage was linked to an almost twofold increased risk of CVD and CVD mortality, a nearly twofold high risk of CHD, a greater chance of CV and an almost twofold increased risk of all-cause mortality.

At 5 years, selective serotonin reuptake inhibitors (SSRIs) were linked to a lower risk of developing diabetes. At 10 years, SSRIs were linked to a higher risk of CV, CVD and all-cause mortality, a lower risk of diabetes and hypertension, and a higher risk of CHD, CVD and all-cause mortality when compared to non-SSRIs.

Mirtazapine, venlafaxine, duloxetine and trazodone caused more adverse effects; however, SSRIs were also associated with an elevated risk.

The studies highlight the importance of proactive cardiovascular monitoring and prevention in patients with depression taking antidepressants, as both have been linked to greater risks.

(*Source: https://www.medscape.com/viewarticle/981951#vp_3*)

Dupilumab Reduces Eczema Symptoms among Infants and Young Children

A phase 3 clinical trial recently reported in *The Lancet* demonstrated that the monoclonal antibody drug dupilumab significantly reduced the symptoms of eczema in children between the ages of 6 months and 5 years old when administered in conjunction with a topical corticosteroid.

Dupilumab's safety and effectiveness were assessed in phase 3 clinical trial on 162 kids with uncontrolled moderate to severe atopic dermatitis between 6 months and 5 years. The study participants either received an injection of the drug and a topical corticosteroid of low potency every 4 weeks or only a topical corticosteroid in the placebo group.

According to researchers, more than half of the patients getting dupilumab showed 75% improvement in their Eczema Area and Severity Index (EASI)-75 after 16 weeks of treatment. The EASI-75 is a scale used by medical practitioners to assess the quantity and severity of inflammatory lesions on the body.

Additionally, after 16 weeks of treatment with dupilumab, researchers discovered that 28% of patients had clean or clear skin, and 48% had a decrease in itching. Some minor side effects, such as conjunctivitis/dry eye condition, were common, and overall the safety profile was very good, but more studies were necessary for dupilumab.

(*Source: https://www.medicalnewstoday.com/articles/new-drug-helped-reduce-eczema-in-75-in-infants-and-young-children#What-is-dupilumab?*)

Ascl1 Protein was Identified to Activate a Group of Genes Related to Cardiomyocytes and Help in Heart Muscle Repair

A recent study has discovered a quicker and more efficient method to rewire scar tissue cells (fibroblasts) into sound heart muscle cells.

Researchers at the University of North Carolina in Chapel Hill have developed a more effective technique for reprogramming scar tissue cells (fibroblasts) to transform them into healthy cardiac muscle cells. Their findings were reported in the journal *Cell Stem Cell* (cardiomyocytes). After a heart attack or as a result of a cardiac condition, fibroblasts create the fibrous, stiff tissue that results in heart failure. The researchers found that fibroblast-to-neuron conversion triggered a set of cardiomyocyte genes. This activation was caused by Ascl1, one of the master-programmer "transcription factor" proteins used to construct the neurons.

Ascl1 triggered the genes for cardiomyocytes; hence upon adding it to the three transcription factor combinations, they had been using to make cardiomyocytes to its effect. They were astounded to discover that Ascl1 had a 10-fold boost in reprogramming efficiency, or the proportion of successfully reprogrammed cells.

(*Source: https://www.hindustantimes.com/lifestyle/health/researchers-identify-protein-partners-that-might-reprogram-scar-tissue-cells-repair-heart-muscle-101665153471213.html*)

Asthma Risk in Children could be Detected Using Childhood Asthma Risk Tool

A team of researchers associated with the CHILD Cohort Study (CHILD) have created an accessible revolutionary symptom-based screening tool to determine the risk of asthma in kids as early as 2 years old.

The efficacy of the tool known as the Childhood Asthma Risk Tool, or CHART was published in the

Journal of the American Medical Association (JAMA). In the study, CHART was used to analyze data from 2,354 children who participated in CHILD, a long-term study that began following about 3,500 Canadian children's physical, social and cognitive development from conception. CHART was able to predict which of these children will have a persistent wheeze by the age of 5, a crucial sign of asthma. The performance of CHART was compared to data from two more cohort studies to confirm the study's conclusions utilizing the CHILD data. This is the first study that, according to the experts, has created a noninvasive technique for the early diagnosis of asthma and persistent wheezing in a general population and that has now been validated in general and high-risk populations.

(*Source: https://www.tribuneindia.com/news/health/new-symptom-based-screening-technique-for-detecting-asthma-risk-in-children-439012*)

Omega-3 may Provide a Brain Boost for People in Midlife

According to a recent study published in *Neurology*, people who consume more omega-3 in their middle years are benefited more than those who consume less omega-3. The study included 2,183 men and women with an average age of 46. The researchers examined the fatty acid profile from the blood samples of each participant and also scanned their brains with magnetic resonance imaging (MRI) technology. Additionally, the individuals underwent neurological examination which evaluated the participants' executive function, thinking, processing speed and delayed episodic memory.

Twenty-five percent of the participants who had omega-3 fatty acids blood levels below 4% were put in the low group, while the rest participants having an omega-3 level of 5.2% were assigned to the higher group. The participants in the higher group had more grey matter and better reading and logical reasoning scores, while those in the lower group were more likely to smoke and have diabetes and were less likely to have a college degree. The study's findings suggest that there may be an association between consuming omega-3 in midlife and an improvement in brain function for adults.

(*Source: https://www.medicalnewstoday.com/articles/omega-3-may-boost-brain-health-for-people-in-midlife-study#Omega-3:Things-to-know*)

Alzheimer's Disease and Normal-Tension Glaucoma

Studies have speculated that glaucoma and Alzheimer's disease share common pathophysiology. Findings of a new retrospective study from Taiwan presented at the American Academy of Ophthalmology (AAO) 2022 Annual Meeting in Chicago has demonstrated an association between the two. According to the new study, over half of the individuals with normal tension glaucoma are likely to develop Alzheimer's disease compared to those who do not have glaucoma.[1,2]

A total of 15,317 patients with normotensive glaucoma diagnoses between January 2001 and December 2013 and age- and sex-matched 61,268 persons as controls were selected for the study from the Taiwan National Health Insurance Database. The patients were followed-up for 13 years (median).

The incidence of Alzheimer's disease in patients with normal-tension glaucoma was 6.7% compared to 4.2% in those who did not have normal-tension glaucoma with an adjusted hazard ratio of 1.52. Patients with normotensive glaucoma had higher prevalence of hyperlipidemia, hypertension, diabetes and coronary artery disease. The risk for Alzheimer's disease remained significant even after adjusting for these variables. Age, female sex and a history of stroke were significantly associated with the risk of Alzheimer's disease among patients with normal-tension glaucoma. No association was found between the various glaucoma medications and Alzheimer's disease.

Normal-tension glaucoma is a subtype of primary open-angle glaucoma, but with normal intraocular pressures. The disease can progress from loss of vision to bilateral blindness. It is often an incidental diagnosis. Clinicians should be aware of the association between Alzheimer's disease and normal-tension glaucoma. All patients of normal tension glaucoma, particularly those at risk, should therefore be screened for Alzheimer's disease.

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2. Source Reference: Chen YY, et al. Association between NTG and the risk of Alzheimer disease. AAO 2022; Abstract PO133. https://www.medpagetoday.com/meetingcoverage/aao/101099.

■■■■

The Scientific Aspects of Prayer

It is natural for us to promise or offer to pray for someone who suffers from sickness. So many people believe in the power of prayer that it has now caught the attention of scientists and doctors. Today most hospitals and nursing homes are building prayer rooms for their patients, based on the principle that a relaxed mind is a creative mind. During prayer, a person is in touch with the consciousness, and is able to take correct decisions. Most doctors even write on their prescriptions "I treat He cures".

Medically it has been proved that the subconscious mind of an unconscious person is listening. Any prayer therefore would be captured by the patient building inner confidence and faith to fight terminal sickness. We have seen the classical example of the effect of mass prayer on a person's health in the case of Amitabh Bachchan's illness.

"Praying for health is one of the most common complementary treatments people do on their own," said Dr Harold G Koenig, co-director of the Center for Spirituality, Theology and Health at Duke University Medical Center.

About 90% of Americans and almost 100% Indians pray at some point in their lives, and when they're under stress, such as when they're sick, they're even more likely to pray.

More than one-third of the people surveyed in a recent study published in the *Archives of Internal Medicine* said they often turned to prayer when faced with medical concerns. In a poll involving more than 2,000 Americans, 75% of those who prayed said they prayed for wellness, while 22% said they prayed for specific medical conditions.

Numerous random studies have been conducted on this subject. In one such study, neither the patients nor the health care providers had any idea who was being prayed for. The coronary care unit patients didn't even know there was a study being conducted. And, those praying for the patients had never even met them. The result: while those in the prayer group had about the same length of hospital stay, their overall health was slightly better than the group that didn't receive special prayers.

"Prayer may be an effective adjunct to standard medical care," wrote the authors of this 1999 study, also published in the *Archives of Internal Medicine*. However, a more recent trial from the April 2006 issue of the *American Heart Journal* suggests that it's even possible for some harm to come from prayer. In this study, which included 1,800 people scheduled for heart surgery, the group who knew they were receiving prayers developed more complications from the procedure, compared to those who had not been a focus of prayer.

Many patients are reluctant and do not discuss this subject with their doctors. Only 11% patients mention prayer to their doctors. But, doctors are more open to the subject than the patients realize, particularly in serious medical situations. In a study of doctors' attitudes toward prayer and spiritual behavior, almost 85% of the doctors thought they should be aware of their patients' spiritual beliefs. Most doctors said they wouldn't pray with their patients even if they were dying, unless the patient specifically asked the doctor to pray with them. In that case, 77% of the doctors were willing to pray for their patient.

Most people are convinced that prayer helps. Some people are 'foxhole religious' types and prayer is almost a reaction or cry to the Universe for help. However, many people do it because they've experienced benefit from it in the past.

If a patient wants to pray and feels it might be helpful, there's no reason he should not. If he believes that prayer might work, then he should use it.

■■■■

INSPIRATIONAL STORY

The Duck and the Devil

There was a little boy visiting his grandparents on their farm. He was given a slingshot to play with out in the woods. He practiced in the woods, but he could never hit the target. Getting a little discouraged, he headed back for dinner. As he was walking back he saw Grandma's pet duck.

Just out of impulse, he let the slingshot fly, hit the duck square in the head, and killed it. He was shocked and grieved!

In a panic, he hid the dead duck in the wood pile, only to see his sister watching! Sally had seen it all, but she said nothing.

After lunch, the next day Grandma said, "Sally, let's wash the dishes." But Sally said, "Grandma, Johnny told me he wanted to help in the kitchen." Then she whispered to him, "Remember the duck?" So, Johnny did the dishes.

Later that day, Grandpa asked if the children wanted to go fishing and Grandma said, "I'm sorry but I need Sally to help make supper." Sally just smiled and said, "Well that's all right because Johnny told me he wanted to help." She whispered again, "Remember the duck?" So, Sally went fishing and Johnny stayed to help.

After several days of Johnny doing both his chores and Sally's, he finally couldn't stand it any longer. He came to Grandma and confessed that he had killed the duck. Grandma knelt down, gave him a hug, and said, "Sweetheart, I know. You see, I was standing at the window and I saw the whole thing, but because I love you, I forgave you. I was just wondering how long you would let Sally make a slave of you."

Thought for the day and every day thereafter?

Whatever is in your past, whatever you have done... And the devil Keeps throwing it up in your face (lying, cheating, debt, fear, bad Habits, hatred, anger, bitterness, etc.) ....whatever it is.... You need to know that God was standing at the window and He saw the whole thing..... He has seen your whole life. He wants you to know that He loves you and that you are forgiven.

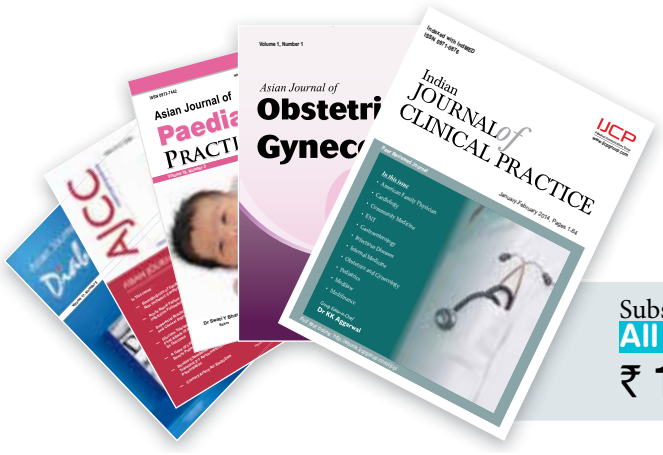
He's just wondering how long you will let the devil make a slave of you.

The great thing about God is that when you ask for forgiveness, He not only forgives you, but He forgets. It is by God's grace and Mercy that we are saved. Always remember: God is at the window.

■■■■

Preventing Atopic Dermatitis in At-Risk Infants

Use of emollients as early as within 1 week of birth may prevent atopic dermatitis in high-risk infants, according to results of the recently published Short-term Topical Application to Prevent Atopic Dermatitis (STOP AD) trial.[1] A total of 321 high-risk infants born at term at Cork University Maternity Hospital (CUMH) were recruited for this randomized controlled trial between April 2019 and November 2020. At least one parent had a positive history of atopic dermatitis (AD), allergic rhinitis or asthma. These infants were randomized to either daily emollient application at 2 weeks, 4 weeks and 8 weeks (intervention group; n = 161) or standard routine skin care (control group; n = 160) within 4 days of birth to examine if early use of emollient could reduce the incidence of AD at 1 year of age. More than 80% of the infants applied the emollient once or twice-daily at the specified time points compared to 68% in the control group. Results published in the journal *Allergy* showed that at 6 months, 18.3% infants in the intervention group developed AD versus 36.4% for the control group. At 12 months of age, nearly 33% infants in the intervention group developed AD compared to 46.4% in the control group. The two groups had comparable incidence of parent-reported skin infections; 5.0% vs. 5.7%, respectively. Based on these findings, the authors concluded that early application of emollient, as early as within 4 days of birth as demonstrated in this single-center study and using it till 2 months was associated with significant decline in the occurrence of AD in at-risk infants. At the same time, the authors also caution that "As we did not collect longer term data, we cannot exclude the possibility that the intervention may have only delayed the onset of AD beyond 12 months". (***Reference:*** *Chaoimh CN, et al. Early initiation of short-term emollient use for the prevention of atopic dermatitis in high-risk infants - The STOP-AD randomised controlled trial. Allergy. 2022 Aug 23*)



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HUMOR

WHAT IT MEANS

Five-year-old Becky answered the door when the Census taker came by.

She told the Census taker that her daddy was a doctor and wasn't home, because he was performing an appendectomy.

"My," said the Census taker, "that sure is a big word for such a little girl. Do you know what it means?"

"Sure! Fifteen hundred bucks and that doesn't even include the anesthesiologist!"

FATHER IS A LAWYER...

While in Atlanta on vacation, Little Johnny's Daddy took one afternoon to see historic sites downtown.

Two young families were also in line to the see the sites. Little Johnny struck up a conversation with one of the boys in line.

"My name is Tommy. What's yours?" asked the first boy.

"Johnny".

"My Daddy's an accountant. What does your Pop do for a living?" asked Tommy.

Little Johnny replied, "My Daddy's a Lawyer."

"Honest?" asked Tommy.

Johnny replied, "No, just the regular kind."

DO YOUR BEST AND JUST REMEMBER

This older man was on the operating table awaiting surgery, and he insisted that his son, a renowned surgeon, perform the operation as he was about to receive the anesthesia he asked to speak to his son. "Yes dad, what is it?"

"Don't be nervous, son. Do your best and just remember, if it doesn't go well and if something happens to me, your mother is going to come and live with you and your wife."

I KEEP THINKING I'M GOD

Doctor, Doctor! I keep thinking I'm God!

Doc: When did this start?

Well first I created the sun, then the earth, then the…

ASSUME WE HAVE A CAN OPENER

A chemist, a physicist, and a mathematician are stranded on an island when a can of food rolls ashore.

The chemist and the physicist come up with many ingenious ways to open the can.

Then suddenly the mathematician gets a bright idea: "Assume we have a can opener …"

A FRIENDLY HONEST NEIGHBOR

A man received the following text from his neighbor:

I am so sorry Bob. I've been riddled with guilt and I have to confess. I have been tapping your wife, day and night when you're not around. In fact, more than you. I'm not getting it at home, but that's no excuse.

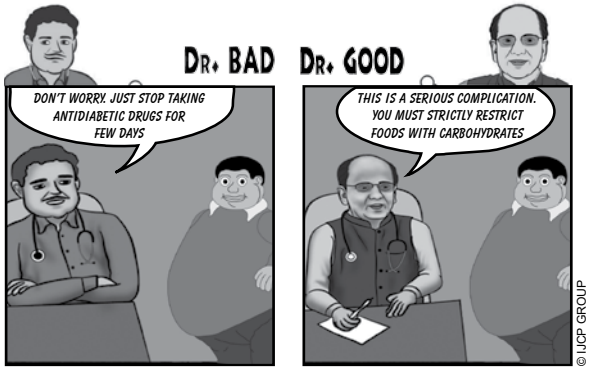
I can no longer live with the guilt and I hope you will accept my sincerest apology with my promise that it won't happen again.

Bob, anguished and betrayed, went into his bedroom, grabbed his gun, and without a word, shot his wife and killed her.

A few moments later, a second text came in: Damn autocorrect. I meant "wifi", not "wife".

Dr. Good and Dr. Bad

SITUATION: An obese patient with T2DM who had recently undergone bariatric surgery experienced hypoglycemia.



LESSON: It has been documented that post-bariatric surgery hypoglycemia is a serious complication, particularly if the patient develops life-threatening neuroglycopenia with loss of consciousness and seizure. The occurrence of this event could be prevented by strict dietary modification including a restriction on intake of carbohydrates and food items with high glycemic index.

Front Endocrinol (Lausanne). 2017;8:37.

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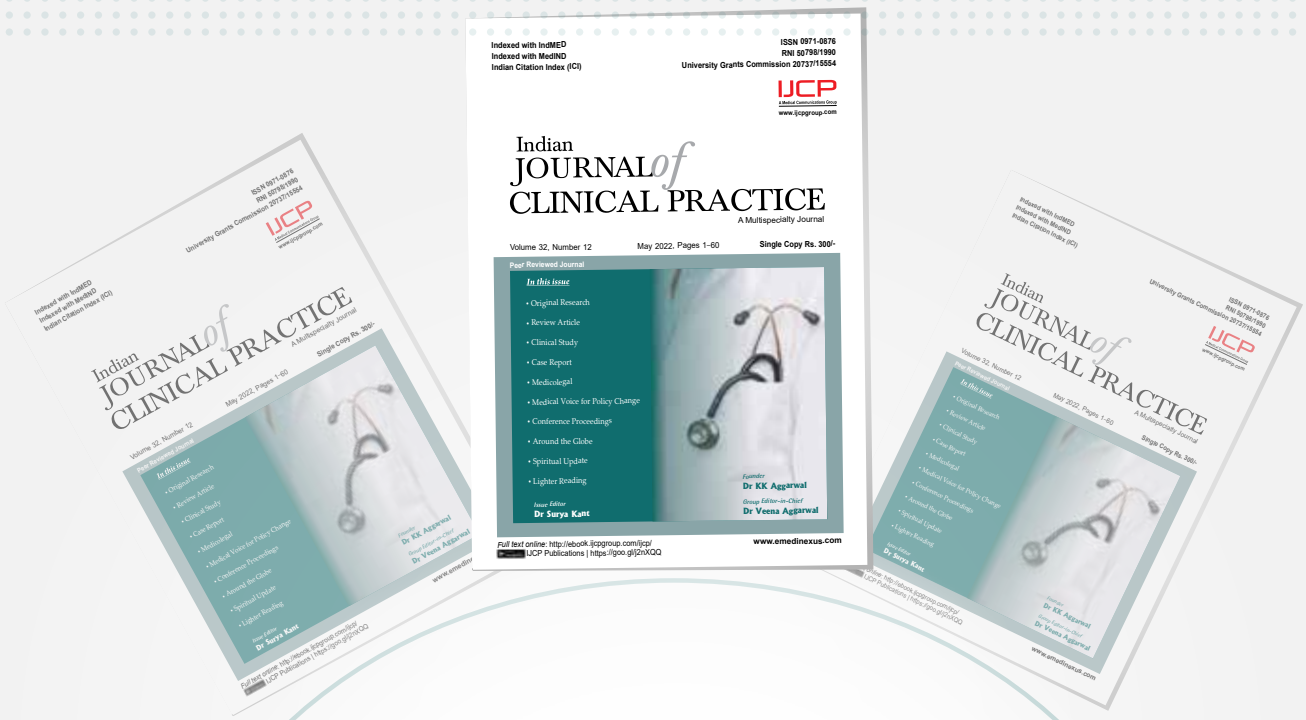

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Paintal AS. Impulses in vagal afferent fibres from specific pulmonary deflation receptors. The response of those receptors to phenylguanide, potato S-hydroxytryptamine and their role in respiratory and cardiovascular reflexes. Q. J. Expt. Physiol.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

Books

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

Articles in Books

Strong MS. Recurrent respiratory papillomatosis. In: Scott Brown's Otolaryngology. Paediatric Otolaryngology Evans JNG (Ed.), Butterworths, London 1987;6:466-470.

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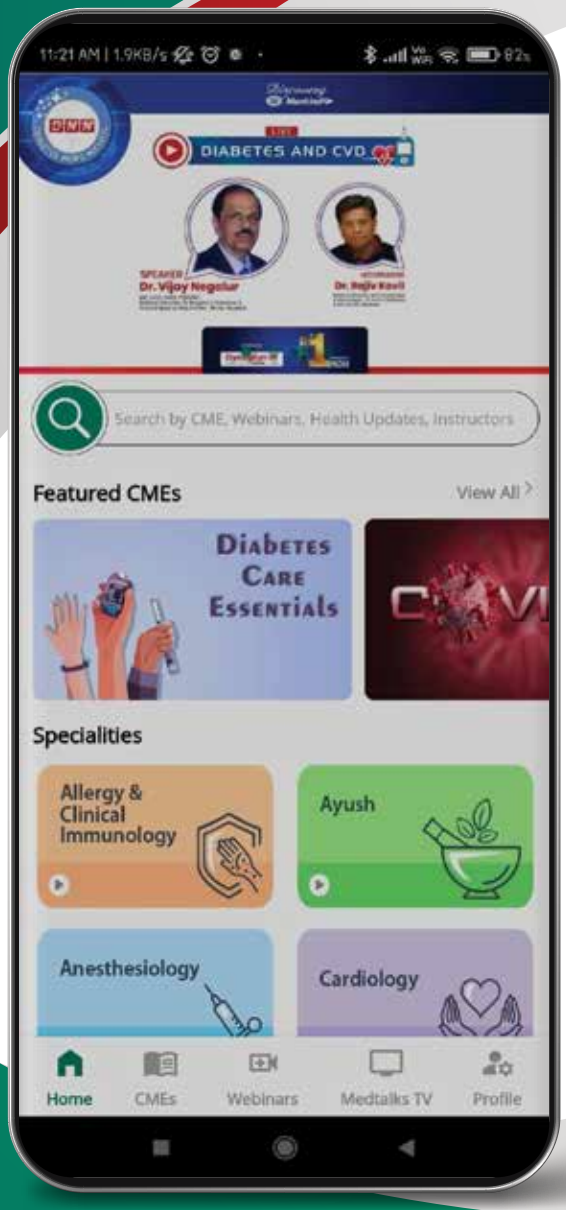

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