

## 24-HOUR PHYSICAL ACTIVITY BEHAVIOURS HELP TYPE 2 DIABETES

(A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD))

This consensus report is geared towards health care providers who are supporting people living with this condition. In addition to encouraging diabetes self-management education and focussing on glycaemic control, the report focuses on other factors that should be considered. One of these is “24-hour physical activity behaviours. **“You might be wondering what this means, and if it involves doing some sort of physical activity or exercise 24 hours a day! It does, to an extent, but not in the way that you might think”.**”

### IMPORTANCE OF 24-HOUR PHYSICAL BEHAVIOURS FOR TYPE 2 DIABETES

#### SITTING/BREAKING UP PROLONGED SITTING

- Limit sitting. Breaking up prolonged sitting (every 30 min) with short regular bouts of slow walking/simple resistance exercises can improve glucose metabolism.



#### STEPPING

- An increase of only 500 steps/day is associated with 2-9% decreased risk of cardiovascular morbidity and all-cause mortality.
- A 5 to 6 min brisk intensity walk per day equates to ~4 years' greater life expectancy.



#### SLEEP

- Aim for consistent, uninterrupted sleep, even on weekends.



**Quantity** - Long (>8h) and short (<6h) sleep durations negatively impact HbA<sub>1c</sub>.



**Quality** - Irregular sleep results in poorer glycaemic levels, likely influenced by the increased prevalence of insomnia, obstructive sleep apnoea and restless leg syndrome in people with type 2 diabetes



**Chronotype** - Evening chronotypes (i.e. night owl: go to bed late and get up late) may be more susceptible to inactivity and poorer glycaemic levels vs morning chronotypes (i.e. early bird: go to bed early and get up early).

#### SWEATING (MODERATE-TO-VIGOROUS ACTIVITY)

- Encourage ≥150 min/week of moderate-intensity physical activity (i.e. uses large muscle groups, rhythmic in nature) OR ≥75 min/week vigorous-intensity activity spread over ≥3 days/week, with no more than 2 consecutive days of inactivity. Supplement with two to three resistance, flexibility and/or balance sessions.
- As little as 30 min/week of moderate-intensity physical activity improves metabolic profiles.



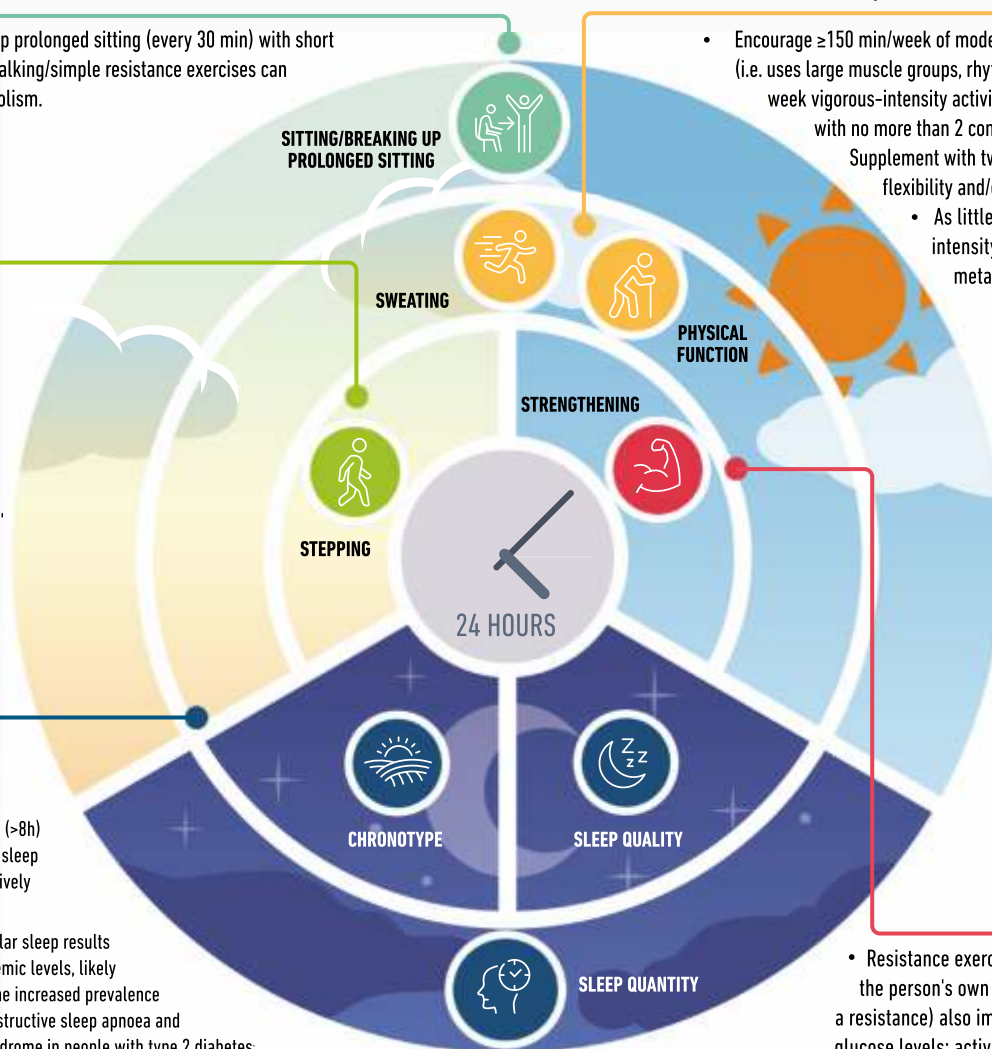
#### Physical function/frailty/sarcopenia

- The frailty phenotype in type 2 diabetes is unique, often encompassing obesity alongside physical frailty, at an earlier age. The ability of people with type 2 diabetes to undertake simple functional exercises in middle-age is similar to that in those over a decade older.



#### STRENGTHENING

- Resistance exercise (i.e. any activity that uses the person's own body weight or works against a resistance) also improves insulin sensitivity and glucose levels; activities like tai chi and yoga also encompass elements of flexibility and balance.



	Glucose/insulin	Blood pressure	HbA <sub>1c</sub>	Lipids	Physical function	Depression	Quality of life
SITTING/BREAKING UP PROLONGED SITTING	↓	↓	↓	↓	↑	↓	↑
STEPPING	↓	↓	↓	↓	↑	↓	↑
SWEATING (MODERATE-TO-VIGOROUS ACTIVITY)	↓	↓	↓	↓	↑	↓	↑
STRENGTHENING	↓	↓	↓	↓	↑	↓	↑
ADEQUATE SLEEP DURATION	↓	↓	↓	↓	?	↓	↑
GOOD SLEEP QUALITY	↓	↓	↓	↓	?	↓	↑
CHRONOTYPE/CONSISTENT TIMING	↓	?	↓	?	?	↓	?

#### IMPACT OF PHYSICAL BEHAVIOURS ON CARDIOMETABOLIC HEALTH IN PEOPLE WITH TYPE 2 DIABETES

↑ Higher levels/improvement (physical function, quality of life); ↓ Lower levels/improvement (glucose/insulin, blood pressure, HbA<sub>1c</sub>, lipids, depression); ? no data available; ↑ Green arrows = strong evidence; ↑ Yellow arrows = medium strength evidence; ↑ Red arrows = limited evidence.

Ref.: Diabetes Care 2022;45(11):2753-2786

**Why does physical activity matter?**

Being physically active is important for everyone, whether they have diabetes or not. But if you have diabetes or even prediabetes, including physical activity in your day should be at the top of your “to-do” list.

It’s important to distinguish between exercise and physical activity, just in case you have visions of needing to hit the gym every day (because you don’t, unless you want to). Exercise is a type of physical activity that is planned, structured, and repetitive and it’s done to acquire health benefits and body fitness. Examples of exercise are:



Physical activity refers to any kind of movements that work your muscles and require more energy than resting. In addition to the types of activity listed above, other forms of physical activity include:



For people with diabetes, being active makes your body more sensitive to insulin, helping you more easily get and keep your blood sugars within your target range. Also, physical activity helps to lower the risk of heart disease, which is a leading cause of death in people with diabetes.

**Physical activity behaviours**

The ADA and EASD Consensus Report emphasizes the importance of regular aerobic exercise (meaning, exercise that involves large muscle groups) and resistance exercise (meaning, using your own body weight or working against a resistance). Both forms of physical activity can improve blood sugars, A1C levels, flexibility, and balance.

But the report also notes that, *“A wide range of physical activities, including leisure time activities, can significantly reduce HbA1c levels. Even small, regular changes can make a difference to long-term health, with an increase of only 500 steps /day associated with 2-9% decreased risk of cardiovascular morbidity and all-cause mortality rates.”* This means that, while carving out time in your day to do some form of physical activity still stands, even small amounts of movement, such as a five-minute walk, can lower the risk of heart disease and increase your life expectancy.

**Your 24-hour physical activity plan**

What might your day look like, then? And what about sleep? Here’s how the consensus report breaks down this 24-hour plan.

**Sitting/breaking up prolonged sitting**

- Too much sitting during the day? Not good. Break it up by doing “short regular bouts” of activity every 30 minutes.
- Try going for a quick walk, climbing the stairs, marching in place, or doing some simple resistance exercises.
- The benefits? Improved blood sugars and lower blood pressure.



**Sweating**

Sweating may not sound too appealing, but sweat or no sweat, getting at least 150 minutes of moderate-intensity physical activity (or at least 75 minutes of vigorous-intensity physical activity) for at least three or more days each week is the goal. Why?

- This level of activity reduces insulin resistance (meaning, helps your insulin work better to control blood sugars), lowers heart disease risk, reduces depression, and helps with managing your weight.
- A brisk walk is an example of moderate-intensity activity, whereas jogging is an example of vigorous-intensity activity.
- A general goal might be to aim to be physically active for at least 30 minutes, five times a week. If 30 minutes sounds like too much all at once, break it up into two 15-minute or three 10-minute segments during the day.



**Strengthening**

Make sure to include two to three resistance, flexibility, and/or balance sessions during the week, as well. Lifting weights, using resistance bands, doing exercises like push-ups, and doing yoga are types of resistance exercises. Stretching, tai chi, and yoga help with flexibility.



**Sleep**

Believe it or not, sleep is included in the 24-hour physical activity behaviours. Getting enough quality sleep is crucial for managing type 2 diabetes. Sleep disorders are common in type 2 diabetes, says the consensus report, and can disrupt quantity, quality, and timing of sleep, as well as contribute to obesity and higher blood sugars. Examples of sleep disorders include sleep apnea, restless leg syndrome, and insomnia.



- Aim for between 6 and 8 hours of consistent, uninterrupted sleep - even on weekends. Too little and too much sleep negatively affects A1C and blood pressure levels.
- If you’re a night owl and sleep late, you are more likely to be less physically active during the day compared with someone who gets up early and goes to bed early, too.
- If you struggle with “sleep hygiene,” meaning, you don’t have daily routines

that ensure you get consistent, uninterrupted sleep, talk with your health care provider to address possible sleep disorders and how to get into a better sleep routine.

The above guidelines are not intended to be overwhelming for you. Instead, these are recommendations for behaviours to fit into your daily routine. You might be doing some of these already! And if not, set goals to work toward them. Keep in mind, too, that while these are intended to help you manage diabetes and promote your heart health, these activities can do so much more: they'll improve your mood, lessen depression, and boost your quality of life.

## MEDICAL DEVICES

### 1. The Cytovale® System:

Cytovale's test gets FDA 510(k) clearance for early sepsis detection. IntelliSep helps clinicians recognise sepsis and make time-sensitive critical decisions. The Cytovale system interrogates thousands of cells per second to rapidly assess host immune state and identify disease signatures. IntelliSep has been designed to help clinicians recognise sepsis and make time-sensitive critical decisions. It provides test results within ten minutes.



Sepsis is the #1 cause of death in hospitals, taking the lives of 270,000 people every year in the United States, which is more than opioid overdoses, prostate cancer and breast cancer combined. Mortality from sepsis increases as much as 8% for every hour that treatment is delayed. As many as 80% of sepsis deaths could be prevented with rapid diagnosis and treatment - making early detection essential.



It is claimed to be the first FDA-approved diagnostic tool for evaluating cellular host response to help identify patients with sepsis in emergency departments. The emergency department-focused tool uses a standard blood sample to provide actionable answers directly. It categorises the patients into three bands according to their probability of the condition.

Band 1 indicates a low probability, with the probability increasing through to Band 3.

The test results can help optimize clinical outcomes and improve hospital resource use. The test was evaluated in a multi-centre clinical validation CV-SQuISH-ED study, which was completed early last year. Findings from previous studies showed the potential of the test for detecting patients at increased risk of sepsis. "Every minute is crucial in identifying sepsis, and IntelliSep has the potential to transform clinical approaches to sepsis triage and diagnosis and save countless lives." Using immune cell morphology, IntelliSep evaluates the immune response of the body to an infection. Run on the Cytovale System, the test can provide valuable new insights related to sepsis.



### 2. TactiFlex and FlexAbility ablation catheters:

TactiFlex ablation catheter, sensor enabled (SE), received a CE mark for treating abnormal heart rhythms such as atrial fibrillation. The company's FlexAbility ablation catheter, SE, also received an expanded indication from the FDA for treating patients with complex heart conditions.



TactiFlex ablation catheter SE has a unique flexible tip and contact force sensing. Its tip design has a laser-cut pattern that flexes when in contact with the heart wall to direct irrigation flow to the treated tissue and to increase catheter stability by up to two times for consistent therapy delivery. The device has proven to reduce procedure times and patients' exposure to radiation compared to standard power ablation. When integrated with the company's EnSite X EP system, physicians can accurately identify areas in the heart that require ablation, deliver high-power, and more easily adapt to the heart tissue than conventional catheters.

"The TactiFlex catheter's data around using high-power during ablation will be game-changing for patients. FlexAbility ablation catheter SE is a flexible tip catheter that helps physicians identify abnormal signals and apply therapy to treat ventricular tachycardia in patients with non-ischemic cardiomyopathy. In its LESS-VT study, 80% of study patients were free from VT for at least six months post-procedure. The data also showed statistically significant improvements in patients' mental and physical quality-of-life measures.

## PRODUCT UPDATE

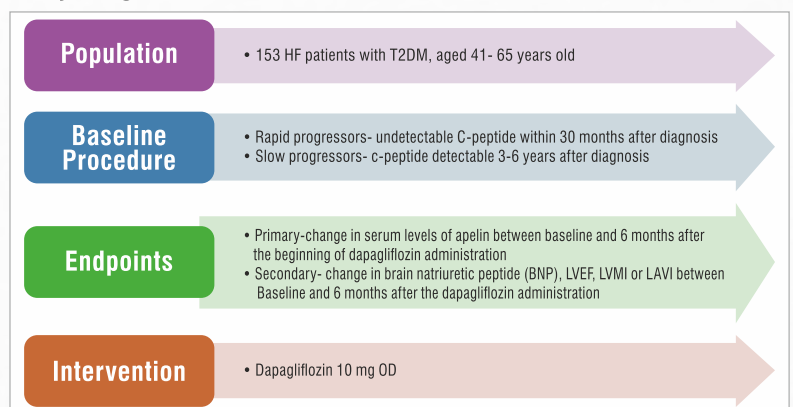
### 1. The Effect of SGLT2 Inhibitor Dapagliflozin on Serum Levels of Apelin in T2DM Patients with Heart Failure:

Apelin is a multifunctional peptide that plays a pivotal role in cardiac remodeling and HF manifestation because of diminishing effects of angiotensin II. It demonstrated positive inotropic and vasodilator effects in both normal and failing hearts in animals. Overall, the levels of apelin may be a promising indicator of cardiac remodeling and biomarker of effective management of HF, T2DM apelin peptides attenuated insulin resistance, improved glucose tolerance and reduced circulating fasting glucose.

However, the impact of SGLT2 inhibitors on circulating levels of apelin remains uncertain.

Study was conducted to investigate the effect of SGLT2 inhibitor dapagliflozin on the levels of apelin in patients with T2DM with different phenotypes of HF.

#### Study Design:



#### Results:

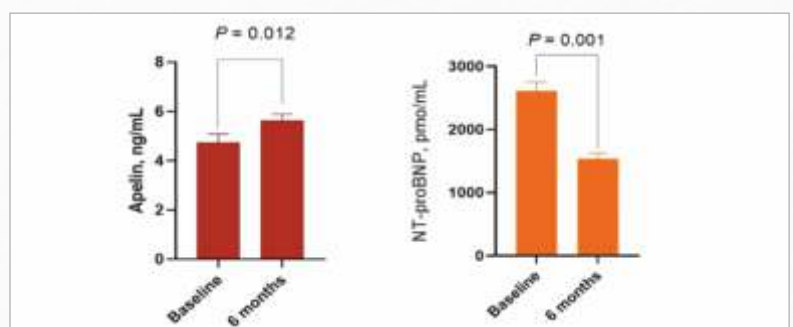


Figure 1 Bar graphs at baseline and 6 months after dapagliflozin administration, showing significant increase in serum levels of apelin (a) and decrease in NT-proBNP (b)

- The administration of dapagliflozin was associated with a significant increase in apelin levels of up to 18.3% and a decrease in NT-proBNP of up to 41.0%
- The levels of apelin demonstrated a significant increase in patients with HFpEF (21.0%)
- 39.5% & 49.3% reduction in NT-proBNP in patients with HFrEF & HFmrEF respectively
- Significant increase in the number of HF patients with II HF NYHA class and decrease in those who had III HF NYHA class. In addition, a significant reduction of LVESV, LVMMI, LAVI was observed

SGLT2 inhibitor dapagliflozin modified the levels of apelin depending on the phenotype of HF, exerting the most meaningful effect in patients with HFpEF. The reproducibility of apelin was higher when compared with NT-proBNP. Moreover, NT-proBNP is considered not to be an optimal surrogate target for the therapy in T2DM with obesity, chronic kidney disease, and HFpEF due to its high serum variability, low diabetes risk and uncertainty in connection with echocardiographic parameters. Acute administration of apelin in HF rapidly increased coronary blood flow, cardiac index, the maximum rate of rise in LV pressure and reduced peak and end-diastolic LV pressures, peripheral artery resistance, and mean arterial pressure.

Study concluded that In T2DM patients SGLT2 inhibition by Dapagliflozin over a 6-month period increases serum apelin levels. Dapagliflozin showed a positive impact on echocardiographic parameters, such as LVEF, LAVI, and E/e'. It led to decrease in serum NT-proBNP levels. It could be a surrogate target for HF management.

**2. Cardiovascular and kidney outcomes of combination therapy with sodium-glucose cotransporter-2 inhibitors and mineralocorticoid receptor antagonists in patients with type 2 diabetes and chronic kidney disease:**

Both sodium-glucose cotransporter-2 (SGLT-2) inhibitors and mineralocorticoid receptor antagonists (MRAs) have been shown to reduce cardiovascular (CV) events in patients with type 2 diabetes (T2D) and chronic kidney disease (CKD).

Hirohichi Wakui, MD, PhD, of Yokohama City University Graduate School of Medicine in Japan, and colleagues performed a systematic review and indirect network meta-analysis of 8 randomized controlled trials involving 36,186 patients. All patients had type 2 diabetes, more than 95% had chronic kidney disease (CKD), and 80% had a urine albumin to creatinine ratio (UACR) greater than 30 mg/g. Of the full cohort, 841 were treated with a combination of an SGLT2 inhibitor and an MRA, 12,046 with an SGLT2 inhibitor alone, 6466 with an MRA alone, and 16,833 with placebo alone. Approximately 86% to 92% of patients also received background treatment with renin-angiotensin-system inhibitors.

The primary outcome in each study was a composite of cardiovascular events, including at least 2 of the following: death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, and hospitalization for heart failure. Combination therapy significantly reduced the risk of the primary outcome by 24% compared with SGLT2 inhibitor monotherapy, 34% compared with MRA monotherapy, and 42% compared with placebo. MRA monotherapy vs placebo was significantly associated with a 2.1-fold increased risk of hyperkalemia.

The combination of SGLT2 inhibitor and MRA significantly reduced the risk of hyperkalemia by 57% compared with MRA monotherapy. Serious adverse events occurred in comparable proportions of each group.

The study concluded that Combination of SGLT-2 inhibitors and MRAs potentially reduced CV events compared with SGLT-2 inhibitors or MRAs alone. This combination may be a candidate treatment strategy for patients with T2D and CKD.

**3. SGLT2I use provide additional protective effects against Obstructive Airway Disease and Exacerbation Events in patients with type 2 diabetes:**

Sodium-glucose cotransporter 2 inhibitors (SGLT2Is) are associated with risk of incident obstructive airway disease (OAD) and exacerbation events in clinical settings among patients with type 2 diabetes compared with dipeptidyl peptidase-4 inhibitors (DPP4Is). Sodium-glucose cotransporter 2 inhibitors (SGLT2Is) are a novel class of antidiabetic medications that confer protective effects on the cardiovascular system and kidneys and possibly the respiratory system. Animal studies have shown SGLT2Is to inhibit NLR pyrin domain containing protein 3

(NLRP3) inflammasome activation in multiple tissues, including the heart, liver, kidney, and lung. Inhibition of the NLRP3 inflammasome has been implicated in both improved asthmatic airway inflammation and COPD exacerbations. Therefore, SGLT2Is may potentially affect OAD.

Retrospective population-based cohort study was conducted in Hong Kong. 30,385 Patients with type 2 diabetes who were prescribed SGLT2Is or DPP4Is were included in this study. Patients were followed for a median of 2.2 years. Compared with DPP4I use, SGLT2I use was associated with a lower risk of incident OAD and a lower rate of exacerbations. The associations were consistent in sex subgroup analysis.

The findings of this retrospective cohort study of patients with type 2 diabetes in Hong Kong suggest that SGLT2I use was associated with a reduced risk of incident OAD and a lower rate of exacerbations in a clinical setting compared with DPP4I use. These findings further suggest that SGLT2Is may provide additional protective effects against OAD for patients with type 2 diabetes.

NEW PRODUCTS				
No.	Brand Name	Generic Name	Approval Date	FDA approved Indication
1.	Filspari	Sparsentan	2/17/2023	To reduce proteinuria in adults with primary immunoglobulin A nephropathy at risk of rapid disease progression
2.	Jesduvrog	Daprodustat	2/1/2023	To treat anemia caused by chronic kidney disease for adults on dialysis for at least four months
3.	Brenzavvy	Bexagliflozin	1/20/2023	To improve glycemic control in adults with type 2 diabetes mellitus as an adjunct to diet and exercise

**Teplizumab-A Ray of Hope for delaying onset of T1DM**

**Dr. Arun Kumar Pande**  
Consultant Endocrinologist,  
Lucknow Endocrine Diabetes and thyroid clinic



Teplizumab injection's approval by the US Food and Drug Administration to stop the evolution of type 1 diabetes for a specific population is being hailed as a potential game-changer.

Type1 Diabetes (T1D) is an autoimmune disease caused by destruction of pancreatic β-cells. This destruction is mediated by the person's immune system and leads to critical deficiency of insulin and 60 percent of those people are youngsters. According to experts, India has the second-highest number of diabetics in the world (77 million estimated), but it also has the most cases of type 1 diabetes (almost 2 lakh estimated cases).

This article discusses the journey of Teplizumab and puts into perspective what makes it a promising agent in the T1D treatment process alongside the emerging pharmacological therapies.

**OKT3 Immunotherapy and realising need for humanised version (Teplizumab)**

The history of Teplizumab development can be traced back to the mid 1970's which saw the advent of B cell hybridoma technology. This pushed the approach of therapeutics development towards mAb immunotherapy. The most successful clinical immunotherapy for T1D has been anti-CD3mAb.

OKT3 is a murine monoclonal antibody of immunoglobulin IgG2a isotype. It was developed in 1979 and received FDA approval as first human mAb immunotherapy for prevention of transplant rejection in 1986. OKT3 worked by blocking both the generation and function of cytotoxic T cells with the selective removal of CD3.

However, its clinical implementation was restricted due to the "flu-like" side effects. The side effects were found to be the result of increased cytokine release from T cells brought by the TCR (T cell receptor)/CD3 complex, induced by OKT3. Further, OKT3, being a mouse monoclonal antibody results in development of human anti-mouse antibody (HAMA).

To help eliminate its fallibility, OKT3 was then humanized by inducing punctual mutations of the Fc thereby preventing binding to FcRs. This genetic engineering stripped off the mitogenic properties of OKT3 and resulted in the genesis of huCD3 $\epsilon$ -directed mAb hOKT3 $\gamma$ 1 Ala-Ala, also known as Teplizumab. Hence came into picture Teplizumab, a humanised version of OKT3 antibody as T1D therapy.

### What is Teplizumab

Teplizumab is a humanised anti-CD3 monoclonal antibody clinically developed by MacroGenics and Eli Lilly. It was developed as an extension of the anti-CD3 therapy traditionally used to prevent graft-versus-host disease. This therapy has been explored to prolong the onset of T1D in high-risk patients. Teplizumab, also termed hOKT3 $\gamma$ 1 (Ala-Ala) and MGA031, was developed by grafting the complementarity-determining region of OKT3 into a human IgG1 backbone. Introduction of two point mutations in its Fc (fragment crystallizable) portion decreases binding to FcR (Fc Receptor) which as a result prevents the activation of the immune system.

### Why Teplizumab and how does it work?

Being a non-activating, Fc-modified anti CD3 monoclonal antibody, Teplizumab works by binding to CD3 of the autoreactive T cells (mediating death of  $\beta$ -cells). Unlike OKT3 which causes the depletion of the autoreactive T cells, Teplizumab causes these cells to migrate to the gut wall and become exhausted.

It is thought that the autoreactive T-cells are pre-active. On receiving additional stimulation by the action of the drug they get pushed towards the exhausted phenotypic stage

**Human Trial-**In 2002, a U.S. based clinical trial was conducted with Teplizumab in phase I/II in patients with anti-islet autoantibodies and recent (within the first 6 weeks of diagnosis) onset of T1D. It was noted that the insulin production was the same or better 1 year post treatment in 9 out of 12 teplizumab recipients versus only 2 of the 12 placebo recipients. Further the glycosylated haemoglobin levels were found to be lower in the patients who had received teplizumab.

These observations thus suggested that  $\beta$ -cells remained intact in people who were treated with teplizumab. (Humanizing Animal Models\_Bresson (2011), n.d.).

**FDA Filing-** Approval from the FDA was filed in July 2021. The antibody endured a rejection however not all was doom and gloomy for the T cell-targeted teplizumab. An advisory committee voted 10 to 7 in favour of the antibody's approval. As per Prevention Bio, rather than safety or efficacy of teplizumab being the concern, it was the need for additional pharmacokinetic / pharmacodynamic (PK/PD) which formed its ground of rejection.

### This shortly triggered the genesis of the PROTECT trial - Recent-Onset Type 1 Diabetes Trial Evaluating Efficacy and Safety of Teplizumab (PROTECT)

PROTECT is a phase 3, randomized, double-blind, multinational, placebo controlled study done to evaluate the efficacy and safety of the (then investigational drug) Teplizumab in children and adolescents with newly diagnosed T1D.

The primary objective of PROTECT involved observing if two courses of Teplizumab administered in a gap of 6 months are able to slow the  $\beta$ -cells destruction and preservation of functional  $\beta$ -cells over the course of 18 months in the (participants/sample); with its secondary objective being the evaluation of improvement in key parameters.

#### Following is used as Primary Outcome measures:

- The area under the time-concentration curve (AUC) of C-peptide after a mixed meal tolerance test (MMTT) at Week 78 [ Time Frame: Week 78 ] Clinical Endpoint

#### Following is used as Secondary Outcome measures:

- Exogenous insulin use [ Time Frame: Week 78 ] Clinical Endpoint
- HbA1c levels [ Time Frame: Week 78 ] Clinical Endpoint
- Time in glycemic target range [ Time Frame: Week 78 ] Clinical Endpoint
- Clinically important hypoglycemic episodes [Time Frame: Week 78] Clinical Endpoint

- Incidence of treatment-emergent adverse events (TEAEs), adverse events of special interest (AESIs), and serious adverse events (SAEs) [Time Frame: Up to Week 52 and Week 78 ] Safety Endpoint
- Teplizumab serum concentrations [ Time Frame: 78 Week ] PK Endpoint
- Incidence and titers of anti-teplizumab antibodies after treatment courses [ Time Frame: 78 Week ] Immunogenicity Endpoint

### Treatment of type 1 diabetes with teplizumab: clinical and immunological follow-up after 7 years from diagnosis (AbATE)

Considering the dearth of work done in the direction of studying long term effects of successful immune therapies for treatment of type 1 diabetes, there was a long-term follow-up study planned, spanning 7years. The Autoimmunity-Blocking Antibody for Tolerance (AbATE) trial was set up to evaluate Teplizumab in individuals with new-onset T1D.

AbATE trial focused on the clinical, immunological and metabolic status of participants after an average follow-up of 7 years.

#### This longitudinal study generated following findings -

- Two courses of teplizumab reduced the decline in C-peptide 2 years after onset of disease.
- In addition to the effects on C-peptide, there was improved HbA1c and insulin use in the drug-treated group.
- A post hoc analysis of the study participants suggested that the responses were dichotomous.
- Where 45% of the drug-treated individuals showed a very robust response and lost less than 10% of their baseline C-peptide response, 55% individuals showed changes in C-peptide that were indistinguishable from untreated control participants.

#### Post a 7 years follow-up

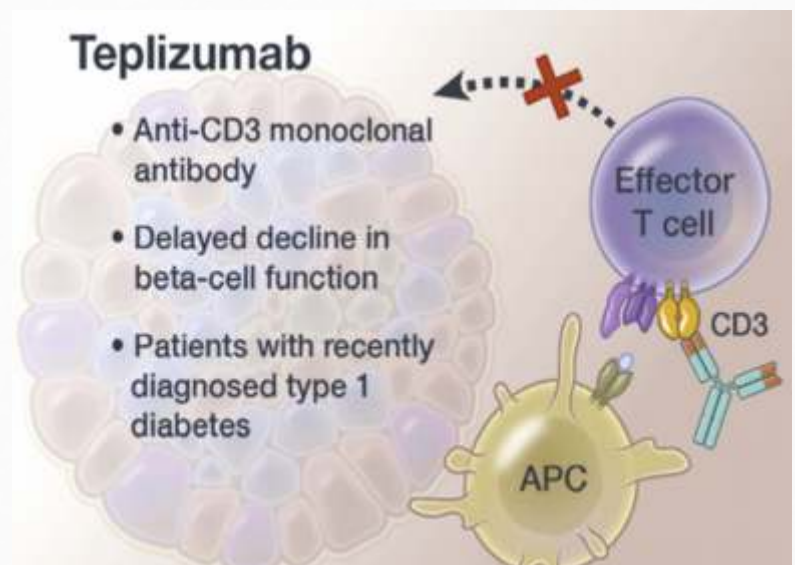
The C-peptide responses to a mixed-meal tolerance test were found to be similar overall in the drug vs. control group of participants. However, they were significantly improved with less loss of C-peptide in drug-treated responders identified at 1 year.

- The improvements in C-peptide response were not associated with lower HbA1c levels or insulin use.
- Drug-treated responders showed a significantly increased frequency of programmed cell death protein 1-positive central memory and anergic CD8+ T cells at follow-up.

#### Teplizumab for prevention of Type 1 Diabetes in Relatives "At-Risk"

This randomized controlled trial published in 2019 in the New England Journal of Medicine suggests possible first-in-class efficacy of teplizumab for prophylactic delay of T1DM onset in high risk patients.

It was a phase 2, randomized, placebo-controlled, double-blind trial of teplizumab involving relatives of patients with type 1 diabetes who did not have diabetes but were at high risk for development of clinical disease. Patients were randomly assigned to a single 14-day course of teplizumab or placebo, and follow-up for progression to clinical type 1 diabetes was performed with the use of oral glucose-tolerance tests at 6-month intervals.



Results from 76 participants who underwent randomization - 44 to the teplizumab group and 32 to the placebo group showed that the median time to the diagnosis of type 1 diabetes was 48.4 months in the teplizumab group and 24.4 months in the placebo group; the disease was diagnosed in 19 (43%) of the participants who received teplizumab and in 23 (72%) of those who received placebo. The annualized rates of diagnosis of diabetes were 14.9% per year in the teplizumab group and 35.9% per year in the placebo group.

This study demonstrated the efficacy of teplizumab in delaying progression to clinical type 1 diabetes in high-risk participants.

**FDA Approval**

FDA however sought more data and clarifications. This led to 3 more years spanning the process which finally reached the denouement on November 17th, 2022 when the antibody secured the FDA approval.

**Tzield has been approved for the following groups of individuals**

- (a) who are 8 years or older
- (b) who have stage 2 type 1 diabetes (with two or more diabetes-related autoantibodies and elevated blood glucose but no symptoms)

Tzield seeks to delay the progression to stage 3 diabetes or clinical type 1 diabetes.

The use of Teplizumab in combination with other forms of cell replacement therapies is advocated for possible prevention of T1D.

**Cost-Benefit Analysis**

A cost-benefit analysis of Teplizumab was published in the Pharmacoeconomics on August 31st, 2020. For this cost effectiveness comparison of the 5 alternatives, Markov microsimulation modelling comparison method was used.

As per the analysis the cost range US\$19,598 - US\$48,956 was found to be a cost-effective option. Probably one of the best benefits is seen with ZnT8 (Zinc Transporter 8) negative, having a cost range US\$88,325 - US\$193,779. Considering the cost of insulin and ketoacidosis it would be beneficial if the cost is between US\$13 850- \$193 900.

**Conclusion**

Teplizumab has evidently been a great contributor in delaying progression to clinical T1D in high-risk participants. The advocates of this monoclonal antibody view it as a pivotal agent that in combination with the cell replacement therapies holds significant potential to pave the way for disease prevention. If teplizumab is priced at or below US\$19,600 it will be the dominant choice for administration to all individuals at risk of developing T1D.

**CASE STUDY - 1**

**Diabetes mellitus with Non healing wound with severe Peripheral Vascular disease.**

**Dr. Sachin Adsule**  
Diabetologist  
Nashik



56 yrs male, known case of Diabetes Mellitus for more than 15yrs, also having Diabetic Retinopathy and Hypertension and Bronchial Asthma. The patient had a personal history of smoking (more than 10/day) for many years, now stopped due to the medical illness.

The patient came with complaints of a Right foot non-healing wound at the base of the 5th toe, dorsal aspect for 2 months. The patient was treated outside but not recovered. Now he was having severe pain and swelling in the RT foot causing difficulty in walking. Inspection showed a cold limb with no pulses to hand or hand doppler. The foot did not show any discoloration or darkness. Color doppler showed significant atherosclerosis with large vessel critical stenosis at the thigh and midfoot level. We suggested PAG and Plasty OR Bypass of the lower limb vessel. Some opinions were for Above-knee or Below-knee Amputation. Due to the delayed decision, the wound became worse with discoloration of the lateral aspect of the foot.

The patient shifted to a higher center where Lower limb Peripheral Angiography and Balloon Plasty along with Thrombolysis were done followed by treatment with the blood thinner was suggested. The patient showed symptoms of decreased pain and redness in the foot.

The patient later started on Local Oxygen Therapy daily for 90 min at our center. 5 Boots were used initially for 10 days (1 boot for 2 days) along with alternate wound dressing with Urgoclean Ag. During this wound showed very impressive changes with decreased pain and discoloration. Pt later was posted for 5th metatarsal head excision and local debridement for removal of high-pressure areas and slough respectively. This was followed by 10 sessions of local oxygen therapy with 5 boots with Advance wound dressing and strict offloading.

This helped the wound to heal. During this pain in the lower limb was reduced very well.

After 58 days of treatment, we could make him walk wound free and **NO AMPUTATION** was done



**PERIPHERAL ANGIOGRAPHY & BALLON ANGIOPLASTY DONE**



**LOCAL OXYGEN FOR 10 DAYS**

**CHANGES IN WOUND APPEARANCE**



**APPLICATION OF URGOCLEAN AG**

**APPLICATION OF URGOSTAT**



CLOSURE OF WOUND



CASE STUDY - 2

An unusual case of primary hypothyroidism presented as massive pericardial effusion

Dr. R. S. Sharma

SSMCH, JBP  
 Consultant Cardiologist,  
 Interventional Cardiologist  
 Medical Specialist & Echocardiologist  
 Specialist in Colour Cardiac & Vascular Doppler  
 Angiography, Angioplasty



**Introduction:** Hypothyroidism is one of the most common hormone deficiencies. It is more common in women. Signs and symptoms of hypothyroidism are lethargy, cold intolerance weight gain, constipation, dry skin, alopecia, hoarse voice, pedal edema, weight gain, bradycardia, and mental retardation. It is an established cause of pericardial effusion, which in turn can be complicated by cardiac tamponade. Here we report a 48-year female without h/o hypothyroidism or cardiovascular morbidity; first presentation with massive pericardial effusion & treated with levothyroxine without pericardiocentesis.

Her pericardial effusion was resolved completely after one month of levothyroxine treatment as evidenced by 2D echocardiography.

**Materials:** A 48-year-old female presented in medicine OPD, with a history of breathlessness on exertion, bilateral lower limb swelling, and hoarseness of voice of 6-month duration. Initially, she had dyspnea on heavy work which later progressed to dyspnea on routine work. On examination, she was conscious-oriented, obeying verbal commands. Dry coarse skin B/L non pitting pedal edema, pulse 60/min, blood pressure 110/80 mm of Hg, heart sound were muffled, ankle reflexes-B/L diminished, SpO2 97% with room air, ECG showed low voltage complex, chest X-ray money bag appearance of heart, and 2D ECHO - massive pericardial effusion with no signs of cardiac tamponade.

**Observation:** Thyroid function tests - T3-21 ng/dl, T4-0.1mcg/dl, TSH 40 IU/L, serum protein- 3.0 g/dl, Other routine laboratory tests were within normal limits. Based on the above findings, the patient was diagnosed with a case of massive pericardial effusion as a complication of primary hypothyroxinemia 75 mcg/day, Tab calcium+ vitamin D3 BD, and Cap Multivitamine one/day. The patient was evaluated by serial 2D Echocardiography. After 15 days of treatment her dyspnea & edema subsided, minimal pericardial effusion on echocardiography & was discharged on Tab levothyroxine 100 mcg/d. After one month of follow-up, the patient was asymptomatic & having no pericardial effusion on 2D echo.

**Conclusion:** Hypothyroidism is very common in India. It is more common in females. Massive pericardial effusion is a rare complication of hypothyroidism. In patients with pericardial effusion even with no symptoms of hypothyroidism, the differential diagnosis should include hypothyroidism, investigated and treated accordingly.

CASE STUDY - 3

Charcot foot case

Dr. Amit Naghate

(DNB Family Medicine, PGP in Diabetology from John Hopkins University, CCD in Diabetology, P. G. Certificate Course in Diabetic Foot Management AIMS, Fellowship in Diabetic foot care and wound care from JIVAS, Organising secretary DFSICON 2016)



Introduction

In India, there are estimated 77 million people above the age of 18 years are suffering from diabetes (type 2) and nearly 25 million are prediabetics. More than 50% of people are unaware of their diabetic status which leads to health complications if not detected and treated early. Combined with reduced blood flow, neuropathy in the feet increases the chance of foot ulcers, infection, and the eventual need for limb amputation.

A diabetic foot is any pathology that results directly from peripheral arterial disease (PAD) and/or sensory neuropathy affecting the feet in diabetes mellitus; it is a long-term (or "chronic") complication of diabetes mellitus. Presence of several characteristic diabetic foot pathologies such as infection, diabetic foot ulcer and neuropathic osteoarthropathy is called diabetic foot syndrome. The resulting bone deformity is known as Charcot foot.

The major challenges relating to diabetes foot are :

1. Foot ulceration is common, affecting up to 25% of patients with diabetes during their lifetime.
2. Over 85% of lower limb amputations are preceded by foot ulcers and Diabetes remains a major cause of non-traumatic amputation across the world with rates being as much as 15 times higher than in the non-diabetic population.
3. Prevention is the first step towards solving diabetic foot problems. Although it was estimated that an ankle is lost to diabetes somewhere in the world every 30 seconds, a more important fact is that up to 85% of all amputations in diabetes should be preventable.
4. Strategies aimed at preventing foot ulcers are cost-effective and can even be cost-saving if increased education and effort are focused on those patients with recognized risk factors for the development of foot problems.
5. Diabetes is now the most common cause of Charcot neuro-arthropathy in Western countries, another condition that should be generally preventable.

What is a Charcot foot?

Charcot foot is a serious complication which can affect persons with peripheral neuropathy, especially those with diabetes mellitus. This is a condition in which the nerves in the lower legs and feet have been damaged. The damage causes a loss of sensation in the feet. It affects the bones, joints, and soft tissues of the foot and ankle. The bones become weak and can break. It has to be treated as early as possible or else the joints in the foot collapse and the foot eventually becomes deformed causing pressure sores to develop in the foot or ankle. An open wound with foot deformity can lead to an infection and even amputation.

What are the signs and symptoms of Charcot foot?

In the early stages, the foot is red, feels warm to the touch, and there is significant swelling of the extremity.

Symptoms

- Swelling or redness of the foot or ankle.
- Skin feeling warmer at the point of injury.
- A deep aching feeling.
- Deformation of the foot.

STAGES OF CHARCOT FOOT

Stage One: Fragmentation and destruction

- This is an acute stage characterized by redness, swelling, warmth of foot and ankle.

- Internally, soft tissue swelling and small bone fractures are starting to occur. The result is destruction of the joints and surrounding bone. This causes the joints to lose stability, resulting in dislocation. The bones may even jellify, softening completely.
- Rocker bottom foot deformity
- Bony protrusions
- If not treated, this stage can last for up to one year.

**Stage Two: Coalescence**

The body attempts to heal the damage done during the first stage. Destruction of the joints and bones slows down, resulting in less swelling, redness, and warmth.

**Stage Three: Reconstruction**

- This is the final stage in which the joints and bones of the foot heal. Unfortunately, they do not go back to their original condition or shape on their own. While no further damage is being done to the foot, it is often left in a deformed, unstable condition.

The foot may also be more prone to the formation of sores and ulcers, which might lead to further deformity or in some cases the need for amputation

**MANAGEMENT AND TREATMENT**

**Medical Management**

- Diabetic Wound Care Management.
- Antibiotic treatment is indicated in all infected wounds in combination with wound care, until the infection is cleared up.
- Hospitalization, immobilisation, and IV antibiotics are indicated for limb threatening or uncontrolled infections.
- Urgent surgery is indicated if the infection is "accompanied by a deep abscess, extensive bone or joint involvement, crepitus, substantial necrosis or gangrene, or necrotising fasciitis. Lepántaloa et al. recommend that "surgical intervention for moderate or severe infections is likely to decrease the risk of major amputation."

**Conservative Management**

It can take several months to treat Charcot foot.

A Charcot restraint orthotic walker (CROW) is used to stabilize the deformities of foot and ankle and minimize bone & joint destruction, it has a rocker bottom sole and total contact design immobilize the joints and allow the patients to ambulate

- Foot cast for 2-3 months
- Walking aids
- Braces
- Prevent new problems
- Wearing shoes that fit feet properly
- Lifestyle modifications

**Surgical Management**

It is done to stabilize any fractured bones or dislocated joints and allow them to heal. A surgeon may also realign or fuse the bones of the foot to better position them to bear weight.

- Exostectomy
- Achilles Tendon Lengthening
- Fusion

**Physical Therapy**

- Physical Therapists are involved in both the prevention and management of diabetic foot complications. This is done by gait, posture, and foot off-loading education and training. The Physical Therapist is also involved in the rehabilitation process after an amputation.

**PATIENT EDUCATION**

**Diabetic Foot Care**

1. Inspect your feet daily. Check for cuts, blisters, redness, swelling or nail problems and inform the doctor if you notice any changes.

2. Bathe feet in lukewarm water.
3. Wash feet using a soft washcloth or sponge. Dry by blotting or patting and carefully dry between the toes.
4. Moisturize your feet but not between toes as it can cause fungal infections.
5. Cut nails carefully.
6. Never treat corn or calluses yourself.
7. Wear clean, dry socks and change them daily.
8. Wear socks to bed.
9. Shake out your shoes and feel the inside before wearing to check for any foreign bodies.
10. Keep your feet warm and dry. Consider using an antiperspirant on soles.
11. Never walk barefoot.
12. Keep blood sugar levels under control.
13. Do not smoke.
14. Get periodic foot exams.
15. Diabetes Complication and Amputation Prevention.
16. Shoes and Orthotics for Diabetics.

**Complications**

- Weak bones
- Deformity: Rocker Bottom
- Toe curls
- Ankle may become twisted and unsteady
- Bones may press against shoes

**PROGNOSIS**

All persons with diabetes who have been treated for Charcot foot should have regular foot care with a foot and ankle specialist or a specialist in diabetic foot problems. Close watch should be done on new changes related to Charcot and other diabetic foot complications. Patients who have Charcot foot from other causes also should have regular follow up as recommended by the doctor.

**CASE DESCRIPTION**

- 40 years old male
- Type2 DM for 15 years OHA recently shifted to insulin
- Nonalcoholic/no tobacco
- Non healing wound on plantar aspect of mid foot for 18 months
- Arterial Doppler normal
- Severe neuropathy Sensitometer40 volts/MHz
- ABI 1.0
- Hba1c 8.3
- Bsl fasting 137, postprandial 270
- Cbc normal, kft normal, ecg normal

Suggestive of sequelae of deformed Charcot foot with calcaneocuboid dislocation





**DIAGNOSIS CHARCOT FOOT**



3D CT Foot reconstruction done to see the bony structure

**How to proceed further**

1. Conservative management
2. Operative intervention

After seeing the CT and considering the ability of the patient to walk we decided to go with surgical intervention as it is done to stabilize bones deformities or dislocated joints and allow them to heal, realign or fuse the bones of the foot to better position them to bear weight.

**Operative highlights**

1. Excision of bony bump
2. TA lengthening
3. Medical column fixation
4. Correction of deformed toes

**POSTOPERATIVE X-RAY**



**SECOND POSTOPERATIVE DAY**



**IMAGE AFTER 5 MONTHS POST OPERATIVE**



**X RAY POSTOPERATIVE 5 MONTHS**



Wound healed completely after 5 months. X Ray showing good fixation and healing. The patient was given customized footwear. Weight bearing started after 6 months.

**TRIAL UPDATE**

**Combining loop with thiazide diuretics for decompensated heart failure: the CLOROTIC trial**

European Heart Journal, Volume 44, Issue 5, 1 February 2023, Pages 411–421  
Published:24 November 2022

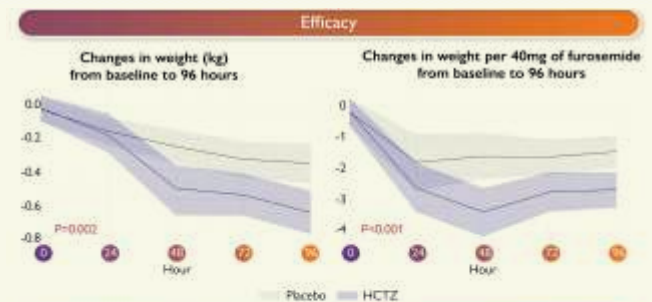
**Structured Graphical Abstract**

Graphical summary of the design and main findings of the CLOROTIC trial

**Key Question**  
Does the addition of a thiazide diuretic to standard intravenous loop diuretic improve the diuretic response in patients with decompensated heart failure (DHF)?

**Key Finding**  
In patients with AHF, the combination of oral hydrochlorothiazide with intravenous furosemide kept diuresis more robust over 96 hours, but was not associated with worsening renal function.

**Take Home Message**  
The addition of hydrochlorothiazide to intravenous furosemide improved the diuretic response in patients with decompensated heart failure at the cost of worsening renal function.



Safety	Placebo	HCTZ	p-value
All-cause mortality at 90 days	19 (16.4%)	23 (20.2%)	0.566
All-cause rehospitalizations at 90 days	40 (34.5%)	43 (37.7%)	0.709
Impaired renal function (serum creatinine and eGFR)	22 (17.2%)	53 (46.3%)	<0.001
Hypotension (SBP < 100 mmHg) - (N&#x2013; < 125 mmHg/L)	6 (5.2%) - 3 (1.7%)	10 (8.8%) - 3 (2.6%)	0.416 - 0.682
Hypokalaemia (K<sup>+</sup> < 3.0 mmol/L) - (K<sup>+</sup> < 2.5 mmol/L)	18 (16.1%) - 0 (0.0%)	43 (46.6%) - 2 (1.8%)	<0.001 - 0.245
Serious adverse events	27 (23.3%)	26 (22.8%)	0.93

**Abstract Aim**

To evaluate whether the addition of hydrochlorothiazide (HCTZ) to intravenous furosemide is a safe and effective strategy for improving diuretic response in acute heart failure (AHF).

**Methods and results**

A prospective, double-blind, placebo-controlled trial, including patients with AHF randomized to receive HCTZ or placebo in addition to an intravenous furosemide regimen. The coprimary endpoints were changes in body weight and patient-reported dyspnoea 72 h after randomization. Secondary outcomes included metrics of diuretic response and mortality/rehospitalizations at 30 and 90 days. Safety outcomes (changes in renal function and/or electrolytes) were also assessed. Two hundred and thirty patients (48% women, 83 years) were randomized. Patients assigned to HCTZ were more likely to lose weight at 72 h than those assigned to placebo [-2.3 vs.-1.5 kg; adjusted estimated difference (notionally 95% confidence interval) -1.14 (-1.84 to -0.42); P= 0.002], but there were no significant differences in patient-reported dyspnoea (area under the curve for visual analogue scale: 960 vs. 720; P= 0.497). These results were similar 96h after randomization. Patients allocated to HCTZ showed greater 24 h diuresis (1775 vs. 1400 mL; P=0.05) and weight loss for each 40 mg of furosemide (at 72 and at 96 h) (P<0.001). Patients assigned to HCTZ more frequently

presented impaired renal function (increase in creatinine >26.5 µmol/L or decrease in eGFR >50%; 46.5 vs. 17.2%; P < 0.001), but hypokalaemia and hyperkalaemia were similar between groups. There were no differences in mortality or rehospitalizations.

**Conclusion:** The addition of HCTZ to loop diuretic therapy improved diuretic response in patients with AHF.

## HEALTHY LIVING

India is presently having the triple burden of undernutrition, obesity and micronutrient deficiencies and also a tsunami of Diabetes. If Rice/wheat, which is the staple food, is replaced with locally grown millets, like Ragi, Bajra, Jowar, we will be ensuring a rich supply of iron to tackle anemia, calcium for bone strength. A significant proportion of proteins to combat protein malnutrition, and a good amount of fiber present will tackle obesity, and is a part of advice for weight loss programmes. Low glycemic index aids in preventing the tsunami of diabetes. (2023 - The International Year Of Millets: Inspiring India to be Swasthyanirbhar)



**Millets**- the super grain that is high in protein, fibre, vitamins and minerals, is often touted as a 'superfood' because of its high nutritional value. As per Ministry of Agriculture and Farmers Welfare, India is a major producer of Millets, accounting for 80% of Asia's production and 20% of global production.

The Government of India sponsored the proposal for International Year of Millets (IYM) 2023 which was accepted by the United Nations General Assembly (UNGA). The declaration has been instrumental for the Government of India to be at the forefront in celebrating the IYM. PM Narendra Modi has also shared his vision to make IYM 2023 a 'People's Movement' alongside positioning India as the 'Global Hub for Millets'



### What are millets:

Millet is a common term for categorising small-seeded grasses that are often called Nutri-cereals. Some of them are sorghum (jowar), pearl millet (bajra), finger millet (ragi), little millet (kutki), foxtail millet (kakun), proso millet (cheena), barnyard millet (sawa), and kodo millet (kodon). An essential staple cereal crop for millions of smallholder dryland farmers across Sub-Saharan Africa and Asia, millets offer nutrition, resilience, income and livelihood for farmers, and have multiple uses such as food, feed, fodder, biofuels and brewing.

### Significance and benefits of millets:

Study finds daily consumption reduces the blood glucose levels. The word 'millets' has become synonymous with healthy food. Recently, it has been found that this food option reduces the risk of Type-2 Diabetes.

A group of researchers, who conducted a study led by the Smart Food Initiative at International Crops Research Institute for the Semi-Arid Tropics (ICRISAT), explored the effect of millets on diabetes and concluded that the percentages of drop in blood glucose levels after consumption of this food remained for a long time.

The study shows that people with diabetes who consumed millets as part of their daily diet saw their blood glucose levels drop 12-15% (fasting and post-meal), and blood glucose levels went from diabetic to pre-diabetes levels.

The HbA1c (blood glucose bound to haemoglobin) levels lowered on average 17% for pre-diabetic individuals, and the levels went from pre-diabetic to normal status.



The researchers have found that millets have a low average Glycemic Index (GI) of 52.7, about 30% lower GI than milled rice and refined wheat, and about 14-37 GI points lower compared to maize. Glycemic Index is a scale that gives an idea about the pace at which a food raises the blood sugar levels. It concluded that even after boiling, baking and steaming, millets had lower GI than rice, wheat and maize. Hence Millets should be part of our staple.

## For Diabetes: Millets Can Be A Game Changer

### Benefits Of Having Millets

Food Safety and Standards Authority of India states that millets are high in nutrition and dietary fibre. It adds that millets contain,

- \* 7-12% protein
- \* 2-5% fat
- \* 65-75% carbohydrates
- \* 15-20% dietary fibre

**FSSAI** also adds that consuming millets also helps fight cardiovascular diseases as millet consumption decreases triglycerides. It states that millets are also known for preventing Type 2 diabetes and reducing blood pressure.

**Indian Institute of Millet Research** states that the fiber present in Millets helps keep "bad" cholesterol in the blood under check and helps protect the heart.

**Millets are one of the healthiest foods on the planet. They are especially a great staple for gluten-intolerant people! Here are some fun facts about millets!**

1. Millet is the generic name given to more than 6,000 species of wild annual grasses found throughout the world.
2. Millet is one of the oldest human foods and believed to be the first domesticated cereal grain. They may have been among the first cultivated crops being grown in the "Hoe Age" preceding the "Plow Age". They were probably first cultivated in Asia more than 4,000 years ago, and they were major grains in Europe during the Middle Ages. Before proper irrigation systems were invented, millet proved to be a very important staple food in African and Asian cultures, due to its drought resistant growth adaptations. Its importance continued until wheat and rice cultivation was perfected.
3. In much of eastern Africa millet is used to make beer.
4. Epidemiological studies have shown that diets rich in millets, including whole grains, are protective against the non-communicable diseases like diabetes, cancer and cardiovascular diseases, due to protective effects of health promoting phytonutrients. Millets are a great staple option for people who are gluten-intolerant.
5. Although its role has diminished, millet still ranks as the sixth most important cereal grain in the world today, sustaining more than one-third of the world's population.

6. Sorghum is grown in nearly 100 countries, and contributes to more than 60% of millets produced globally.
7. Pearl millet is the most drought and heat tolerant of all cereals, being associated with cultivation in high temperatures, light soils and semi-arid growing conditions.
8. Finger millet has the highest productivity of (1640 kg/ha) among the millets in India.
9. Proso millet contains the highest amount of proteins (12.5%).
10. Barnyard millet is the richest source of crude fibre and iron.
11. Foxtail millet has a low water requirement and is successful almost entirely due to its short growing season. It matures in 65-70 days.
12. Millets are a rich source of fibre, minerals like magnesium, phosphorus, iron, calcium, zinc and potassium.
13. Enriched with iron, protein and fibre, jowar (sorghum) can help in reducing cholesterol level. It is good for people who have wheat intolerance.
14. Finger-millet (Ragi) is a healthy substitute for rice and wheat. Loaded with protein and amino acids, this gluten-free millet is good for brain development in growing children.
15. Foxtail millet (Kakum/Kangni) has healthy blood sugar balancing carbohydrates and it is popularly available in the form of semolina and rice flour. The presence of iron and calcium in this millet helps in boosting one's immunity.
16. Pearl millet (Bajra) is rich in iron, protein, fibre, and minerals such as calcium and magnesium which help keep the heart healthy. It is also rich in potassium which dilates blood vessels, allowing blood to flow more easily. This helps reduce overall blood pressure.
17. Barnyard millet (Sanwa) has high fibre content, which can effectively help in losing weight. It is a rich source of calcium and phosphorus, which helps in bone building.
18. Proso / Broomcorn millet (Chena) can effectively help in balancing blood sugar level.
19. Little millet (Moraiyo / Kutki / Shavan / Sama) Packed with B -Vitamin minerals like calcium, iron, zinc and potassium, little millets can provide essential nutrients, which help weight loss. Its high fibre content makes it a healthy replacement for rice.
20. Amaranth (Rajgira / Ramdana / Chola) has a great protein content; it is high in calcium and full of antioxidants and minerals. It helps prevent hair loss and greying. It lowers cholesterol and the risk of cardiovascular disease.
21. Whole-grain Buckwheat (Kuttu) can be very helpful in weight loss. It is diabetic friendly, reduces Blood Pressure and promotes good cardiovascular health. It is also known to provide protection against breast cancer, childhood asthma and gallstones.
22. Kodo millet (Kodon) is very easy to digest, it contains a high amount of lecithin and is excellent for strengthening the nervous system. They are rich in B vitamins, especially niacin, B6 and folic acid, as well as the minerals such as calcium, iron, potassium, magnesium and zinc. Kodo millets contain no gluten and are good for people who are gluten-intolerant and people suffering from high blood pressure and high cholesterol levels.

**We hope you enjoyed these amazing facts about millets and you take a definite step towards adding them to your diet to fulfill your nutritional needs.**

Here are some simple, delicious & healthy millet recipes

### Pearl Millet Pakoda

**Ingredients:** Chopped onion, green chilli; pearl millet flour - 1 cup, bengal gram flour - 1/2 cup; chilli powder and salt-as required.

#### Preparation Method:

- Mix pearl millet sorghum flour, bengal gram flour, chopped onion, green chilli, chilli powder, salt and water with medium batter consistency.
- Fry the batter in oil with the required shapes.
- Excess oil is removed in a tissue.
- This is served as an evening snack along with tomato sauce.



### Finger Millet Cake

**Ingredients:** Finger millet flour- 100g, essence - 3ml, fat - 100g, baking powder - 3g, egg - 2, cocoa powder - 5 g, sugar - 100g, salt - 2 g and milk - 20ml

#### Preparation Method:

- Pre heat oven to 180°C, sieve all dry ingredients thrice for uniform mixing.
- Sugar powder and egg whites are to be beaten well and add milk, essence, egg yolk and mix well.
- Add finger millet flour, salt, cocoa powder and baking powder and make into fine batter.
- Put the batter in a baking bowl and place in the oven at 180°C for 25- 30 min.
- Take the cake out and wait for 10 min until it cools.
- The cake is removed from the mold after atleast 15 min. cut into pieces and serve.



### Barnyard Millet Cutlet

**Ingredients:** Dehulled barnyard millet grains - 100g, potatoes - 20g, carrots - 20g, beans - 20g, salt - 5g, pepper - 5g, chat masala - 5g, bread crumbs - 20g, channa dal - 30g, green chillies - 5g, water - as required and oil - for shallow or deep frying

#### Preparation Method:

- Cook barnyard millet in boiling water and fluff it with a fork and keep it aside.
- Mix chana dal flour powder with curd, boil the vegetables and saute finely chopped onions, green chilli, garlic, ginger and saute until onions turn transparent in oil.
- Add salt, pepper powder, turmeric powder to the cooked vegetables and add cooked barnyard millet, finely chopped coriander leaves and mix well. Cook for a further few seconds.
- Leave it to cool. Divide the mixture equally and shape into cutlet and shallow fry the cutlets on both sides until golden brown or deep fry them in oil.
- Serve with sauce.



### Barnyard Millet Pizza

**Ingredients:** Pizza base: Barnyard millet, 1/2 cup, maida - 1/2 cup, baking soda - 1/2 tsp, salt-as required, oil-1/2 tsp (for cooking the crusts),water-if needed; millet crust pizza-Onions, green capsicum, tomatos cubed-1/3cup, sweetcorn kernels-a few tomato sauce-1/3 cup and mozzarella cheese-as required

#### Preparation Method:

- Soak the millet in enough water for at least an hour and grind into a smooth paste.
- Add baking powder, maida along with salt and mix well (you can also ferment the batter in a warm place for 6 hrs)
- Heat a flat pan. Pour a ladle full of the prepared batter - don't spread it. Spread a few drops of oil all around the crust, cook and flip it to the other side.
- Pre-heat the oven at 180°C for about 5-7 mins.
- Meanwhile, line a baking tray with aluminum foil or parchment paper. Place these prepared pizza crusts on the baking tray.
- Spread the tomato sauce and mozzarella cheese over the sauce. Place cubed onions, capsicum and sweetcorn all over the pizza.
- Bake/Grill at 180°C for about 7-10 mins, until the cheese is bubbly and the vegetables are toasted.
- Serve hot with red chilli flakes and mixed Italian herbs on top!



**NOTE:** There can be a few cracks over the edges of the pizza crust as it is gluten free, but that not hamper the taste

## RESTORED THE SPARK

'I was giving CPR training session organized by Aprica Healthcare Ltd. One of the attendees suddenly collapsed, and I knew that time was of the essence. He was a 62-year-old man, who lost consciousness and there was an absence of pulse, I immediately began performing CPR, providing compressions to pump the patient's heart and rescue breaths to revive it. The other bystanders had already called the ambulance. One of my paramedical staff also joined me and we continued giving CPR for about 45 minutes.

Thankfully, our efforts paid off, and the patient regained consciousness and was rushed to the hospital for further treatment.



The incident served as a stark reminder of the importance of learning CPR and being prepared for emergencies.

I am grateful to companies like Aprica Healthcare Ltd who come up with such good initiatives for training the general public and paramedical staff in CPR and AED. As a trained medical professional, I urge everyone to take CPR training courses and learn the basics of first aid. It's a small step that can make a big difference in someone's life.'

**Dr. S. S YADAV** M. D, D. cardio  
Director of Jaipur Heart & General Hospital

**91.8%**  
people die outside hospital  
due to sudden cardiac arrest<sup>1</sup>



**CPR**  
can triple the chances of a  
person's survival<sup>2</sup>



With the  
**"Heart Hero"** initiative

Conducted **5000+** CPR  
programs and trained  
**150000+** "Heart Heroes"



**3000+** healthcare professionals  
have joined our mission to  
save lives

Join our mission and together lets build an army of  
**"Heart Heroes"** to save lives



## LEND A HAND SAVE A LIFE!

Every year, millions of Americans are trained on how to perform CPR, yet only a few actively step in when they see someone experiencing sudden cardiac arrest. According to the American Heart Association, only 32% of out-of-hospital cardiac arrest (OHCA) victims receive CPR from bystanders. Another study, published in Circulation, revealed that among 10,000 OHCA cases, only 22.1% of those who received bystander CPR survived.

Countries like the United States, Europe, Japan and Singapore have mandated hands-only CPR in their school curriculum as well as private sectors while in India such a policy step still seems far away.

In India less than two per cent people are aware or know the technique of CPR. Reports show that about 4,280 people out of 1 lakh people suffer from cardiac arrest every year in the country. Deaths due to the cardiac arrests are above 53% with each year. Every minute 112 people are succumbing to cardiac arrest. Furthermore, during the last decade, we have seen an increase in heart illnesses among young people aged 20 to 25. This is a concerning issue.

According to data, around 80 to 82 percent of cardiac arrests occur outside of a hospital. Every minute, the odds of survival drop by 7 to 10%. The initial 5-6 minutes after a person develops SCA are critical. Many patients don't get medical help during this time. Administering Hands Only CPR within this time can save the life of about 50% of the patients. Any cardiac arrest that goes beyond 7 minutes can put the patient to risk. This is what the public has to be made aware of. Since time is important, any layman or bystander can save a life with a skill which can be learned with a practice of 5-10 minutes.

Aprica Healthcare Ltd has pledged to promote and contribute to this social cause. In order to achieve this goal, we launched the HEART HERO campaign in 2018. The initiative's purpose was to train as many individuals as possible in CPR techniques and raise awareness about the need of CPR and AED use in emergency situations.

Since the inception of our initiative, we have conducted more than 5000 CPR programs and trained more than 150000 individuals. Over 3000 healthcare professionals have joined us in this life-saving mission. We have disseminated educational materials such as posters and leaflets in addition to the training sessions to promote awareness about the need of CPR. We would want to express our gratitude to all those who have participated in our CPR training sessions and helped spread the word about our initiative.

We are excited to announce that Aprica does not intend to stop here. We are taking a step forward with our mission. We are launching **HEART HERO 2.0**, an upgraded campaign, equipped with advanced CPR training devices and facilities, aimed at reaching out to more people, schools, hospitals and public sectors across the country. We believe this new iteration will serve the purpose of training and raising awareness regarding CPR and equip more people with life-saving skills. We're thrilled to invite you to join us in this campaign. As we work towards our goal, we believe that it's crucial to have a community of like-minded individuals who share our vision. We want you to be a part of this journey and to help us make a real impact.

So come on board with us, together we can empower the nation with the knowledge and skills to perform CPR, thus making a positive impact on the health and well-being of the society.

**Dr Ashitha George Joseph**  
Medical Advisor  
Aprica Healthcare Ltd

