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U.S.'s heavy duty attack on Iran's nuke sites

Apart from the B-2s and the bunker busters, were other weapons used in the recent military strike by the U.S. against Iran? Why are the B-2s maintenance intensive? Why were the Massive Ordnance Penetrator (MOP) 'bunker buster' bombs needed? Is the U.S. already manufacturing new stealth bombers?

EXPLAINER

Dinakar Peri

The story so far:

On June 21, U.S. President Donald Trump announced that the U.S. military carried out precision strikes on three key Iranian nuclear facilities, mainly Fordow, Natanz and Isfahan. He further stated that the strikes were a "spectacular" military success and that Iran's key nuclear enrichment facilities have been "completely and totally obliterated". The key part of these strikes were conducted by the B-2 Spirit stealth bombers which dropped GBU-57 bunker busters to penetrate the Fordow enrichment facility located deep inside a mountain, that was beyond the capability of Israel. Later on Sunday, U.S. Secretary of Defence Pete Hegseth and Gen. Dan Caine, Chairman of the Joint Chiefs of Staff detailed the strikes carried out by the U.S. Central Command (Centcom) under 'Operation Midnight Hammer'.

How were the strikes carried out?

After proceeding quietly and with minimal communication for 18 hours from the U.S. to the target area, the first of the seven B-2 Spirit stealth bombers dropped two 30,000 lb GBU-57 Massive Ordnance Penetrator (MOP) 'bunker buster' bombs at the Fordow site at approximately 6:40 p.m. EDT, Gen. Caine told media houses. The initial mission package also included several decoy aircraft that flew west over the Pacific Ocean as "a deception effort known only to an extremely small number of planners and key leaders here in Washington," he stated.

"The U.S. employed several deception tactics – including decoys – as the fourth and fifth generation aircraft pushed out in front of the strike package at high altitude and high speed, sweeping in front of the package for enemy fighters and surface-to-air missile threats", according to Gen. Caine. "Following the initial strike on Fordow, the remaining B-2s went on to deploy their ordnance, eventually totalling 14 MOPs hitting the targeted areas," he said noting that this was the first operational use of the GBU-57 MOP.

In addition to the MOPs, a U.S. submarine launched more than two dozen Tomahawk land attack cruise missiles at key infrastructure targets at the Isfahan site, bringing the overall total of precision-guided weapons employed during the operation to approximately 75. "Initial battle damage assessments indicate that all three sites sustained extremely severe damage and destruction," Gen. Caine stated, although later in the day several U.S. officials expressed doubts on the extent of damage to the Fordow facility.

What is a B-2 stealth bomber?

The U.S. Air Force (USAF) operates the country's bomber fleet which consists of 114 B-1 Lancers, 21 B-2 Spirit and 137 legacy B-52 aircraft. Of these, B-2 is the only fully stealth aircraft while the B-1 has some stealth features. Each B-2 costs over $2 billion, the most expensive aircraft ever, and so only 21 aircraft were built. One B-2 crashed in 2008 while another was damaged in 2022, and with the repair work deemed prohibitive, it is set to be retired soon. This leaves only 19 B-2 aircraft in active inventory.

The B-2 has always inspired awe with its bat-like shape, and has been extensively showcased by Hollywood. It is a dual-capable multi-role heavy bomber, powered by four engines. According to the USAF, the B-2's low observability is derived from a combination of reduced infrared, acoustic, electromagnetic, visual and radar signatures. "These signatures make it difficult for sophisticated defensive systems to detect, track and engage the B-2," the USAF states. The B-2 made its first flight in 1989 and began operations in 1997. With a crew of two, it can carry a payload of 40,000 lb, has an un-refuelled range of 6,000 miles and a service ceiling of 50,000 feet. It is 69 feet long, 17 feet high and has a wingspan of 172 feet, half the length of a football field.

For Sunday's mission, the B-2s flew 37-hours non-stop, from their home base to the target location and back, re-fuelling several times mid-air, making it the second longest mission ever. The B-2s hold the record for the longest air combat mission in history. As per its manufacturer Northrop Grumman, in 2001, six B-2s were the first to enter Afghan airspace for a record setting 44-hour mission. According to an article in the *New York Post*, the B-2 pilots "have their cockpits outfitted with mini refrigerators and a microwave oven to keep their crew fed and alert" and also have a toilet and enough space for one person to lay down and rest.

A March 2025 report of the U.S. Congressional Research Service (CRS) states that the USAF continues to modernise the B-2. Northrop Grumman was awarded a contract in 2024 of up to $7 billion to maintain and improve B-2 stealth and communications capabilities, engines, and displays through 2029.

The B-2s are extremely maintenance intensive. According to a detailed account in *The Atlantic* on the B-2s employed in Libya in 2018, 100 hours of maintenance were required for every hour of flight. This is mainly because the advantage of stealth is B-2's edge, and it is achieved by design and radar-absorbing materials. To maintain them, the aircraft needs temperature controlled hangers to protect against changes in temperature, humidity, and dust.

Sleek design: A B-2 stealth bomber flies over the Washington Monument, on July 4, 2020. AFP

Why was there a need for 'bunker-busters'?

The nuclear fuel enrichment site at Fordow is located 60 miles south of Iran's capital Tehran in the mountainous region close to the city of Qom. The facilities are buried deep underground, estimated to be 80-90m deep, to withstand Israeli airstrikes. Iran acknowledged its existence only in 2009. That's why there was a need for the GBU-57 MOP and the B-2 Spirit that can carry it. It also meant that the U.S. had to officially enter the Israel-Iran conflict which began on June 13, when Israel started bombing Iranian nuclear and military facilities.

The GBU-57 MOP, according to the USAF is a weapon system designed "to accomplish a difficult, complicated mission of reaching and destroying our adversaries' weapons of mass destruction located in well protected facilities." It is more powerful than its predecessor, the BLU-109 and the GBU-28. According to USAF, a total of 20 MOPs were contracted. The B-2 Spirit is the only aircraft in the USAF capable of employing the 20.5 ft, 30,000 lb MOP which is guided by GPS to reach and destroy targets. Given the weight, each B-2 can hold two MOP bombs.

According to a 2012 CRS report, the GB-57 has a penetration capability of up to 200 feet underground before exploding. "By some reports, it was expected to penetrate as much as 200 feet through 5,000 psi reinforced concrete, and 25 feet into 10,000 psi reinforced concrete," it states. The *New York Times* quoted a senior U.S. official who stated that the strike on the Fordow site did not destroy the heavily fortified facility but has severely damaged it, taking it "off the table." The person noted that even 12 bunker-busting bombs could not destroy the site.

What next?

This mission was not, and has not been, about regime change, Mr. Hegseth said. "The president authorised a precision operation to neutralise the threats to our national interests posed by the Iranian nuclear program and [in support of] the collective self-defense of our troops and our ally, Israel." However, it is unclear whether the objectives of fully neutralising the nuclear enrichment facilities of Iran has been accomplished. Moreover, the whereabouts of the enriched uranium are unknown, as per U.S. officials.

A next generation bomber, the B-21 Raider, a dual-capable penetrating-strike stealth bomber, is currently under development. The B-21 is similar to the B-2, but slightly smaller, with a distinctive beak domed centre. According to a USAF fact sheet, the B-21 has been designed with an open systems architecture to allow for faster new software integration. With a plan to make them enter service in the next few years, the USAF is looking at acquiring a minimum of 100 aircraft at an average unit procurement cost of $550 million.

THE GIST

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The need for gender equity in urban bureaucracy

India is in the midst of a profound urban transformation. By 2050, over 800 million people, about half the population, will live in cities, making India the largest driver of global urban growth. As cities expand spatially, economically and demographically, they are rewriting the social contract of a modern India and shaping the future of its democracy and development.

In the last three decades, progressive constitutional reforms have advanced gender equity. The 73rd and 74th Amendments mandate 33% reservation for women in Panchayati Raj Institutions (PRIs) and Urban Local Governments (ULGs), further strengthened to 50% by 17 States and a Union Territory. Today, women comprise over 46% of local elected representatives (Ministry of Panchayati Raj, 2024), as a rising presence of mayors and councillors.

However, the bureaucratic apparatus that implements their decisions remains overwhelmingly male. While women's representation in grass-root politics has increased, administrative cadres (city managers, planners, engineers, police) exhibit a stark imbalance, limiting the ability of cities to respond equitably to all citizens. As we invest in highways, metros, and smart cities, we overlook a foundational aspect of inclusive development – gender equity in bureaucracy.

The bureaucratic gender gap

Despite more women entering the civil services, the urban administrative architecture remains male-dominated. As of 2022, women constituted just 20% of the Indian Administrative Service (IndiaSpend-2022), with even lower representation in urban planning, municipal engineering and transport authorities. In policing, only 11.7% of the national force are women (Bureau of Police Research and Development-2023), and often confined to desk roles.

This gap is cause for concern. In cities, the engagement of women is different. They rely more on public transport, make multi-stop journeys for work and caregiving, and depend on neighbourhood-level infrastructure. An Institute for Transportation and Development Policy and Safetipin study found that 84% of women in Delhi and Mumbai used public or shared transport; it was 63% for men. Yet, urban planning prioritises mega-projects over safe, accessible, neighbourhood-level mobility. A 2019 Safetipin audit across 50 cities found over 60% of public spaces were poorly lit. With few women in policing, community safety initiatives often fail to resonate with women.

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In India, while women's representation in grass-roots politics has increased, administrative cadres tell a different story

This underrepresentation is not superficial; it affects outcomes. Women officials bring perspectives shaped by lived realities. Studies by the Indian Council for Research on International Economic Relations and UN Women show that they prioritise water, health and safety, and improve public trust in law enforcement through empathetic enforcement. Gender-sensitive design requires gender-diverse institutions.

Missed opportunity in gender budgeting

Gender-responsive budgeting (GRB), which integrates gender considerations into public finance, is a promising but underutilised tool in India's urban governance. Introduced globally in the 1990s, GRB recognises that budgets are not neutral and can reinforce inequities if left unchecked.

India adopted a Gender Budget Statement in 2005-06, with Delhi, Tamil Nadu and Kerala leading efforts. Delhi has funded women-only buses and public lighting; Tamil Nadu applied GRB across 64 departments in 2022-23, and Kerala embedded gender goals through its People's Plan Campaign. Yet, studies by UN-Women and the National Institute of Public Finance and Policy show that most such efforts suffer from weak monitoring and limited institutional capacities, especially in smaller cities. For many ULGs, GRB remains tokenistic, overlooking essentials such as pedestrian safety or childcare in urban planning.

In contrast, countries such as the Philippines mandate 5% of local budgets for gender programmes; Rwanda integrates GRB into national planning with oversight bodies; Uganda mandates gender equity certificates for fund approvals; Mexico ties GRB to results-based budgeting; and South Africa pilots participatory planning to anchor GRB in lived realities. These are not just fiscal reforms but also a reimagining of citizen-centric governance in cities.

Building inclusive cities requires moving beyond political quotas to ensure women's presence in bureaucracy. This demands systemic reforms in recruitment, retention and promotion across administrative and technical roles. Affirmative action, through quotas and scholarships in planning and engineering, is key to dismantling structural barriers.

Globally, countries as varied as Rwanda, Brazil, and South Korea show the impact of representation. Rwanda boosted maternal health and education spending; Brazil prioritised sanitation and primary health care; South Korea's gender impact assessments reshaped transit and public spaces and Tunisia's parity laws gave women more technical roles, improving focus on safety and health. The Philippines uses gender-tagged budgeting to fund gender-based violence shelters and childcare. Gender-balanced bureaucracies are not about fairness alone. They are essential for building safer, equitable, responsive cities.

The cities we deserve

As India aspires to become a $5 trillion economy, its cities must also aspire to be more than economic growth engines. They must become spaces of inclusion and equity. Gender must be mainstreamed into planning and implementation through mandatory audits, participatory budgeting, and linked evaluation. GRB should be institutionalised across ULGs, supported by targeted capacity-building.

Representation must also translate into agency, and help dismantle glass ceilings. Local gender equity councils and models such as Kudumbashree offer templates, especially for small and transitioning cities. Women are already reshaping governance as elected leaders. They must now shape how cities are planned, serviced and governed. When cities reflect women's lived experiences, they work better for all. To build cities for women, we must start by building cities with women.

Nuclear spectre

Israeli and U.S. actions against Iran amount to nuclear brinkmanship

After a 12-day intense missile barrage and air attacks following Israel's illegal aerial attacks on Iran, the two countries finally announced a ceasefire on Tuesday. Ostensibly conducted as a "pre-emptive" strike on Iran's nuclear facilities, the Israeli attacks graduated into a full-fledged war that also involved U.S. strikes on Iranian nuclear installations. These attacks, in blithely ignoring the dangers of radioactive leakage, and their subsequent responses, point to the stark nature of a fragile international order now threatened by escalating nuclear risks from West Asia to Ukraine and even the Indian subcontinent. The attacks on Iran might have damaged its nuclear installations and, in particular, its uranium enrichment capabilities. Yet, this naked aggression was against a signatory to the Nuclear Non-Proliferation Treaty (NPT) and a country that had willingly subjected its facilities to international scrutiny. Iran had also signed the Joint Comprehensive Plan of Action with the P5+1 (nuclear-armed states plus Germany) to ensure that its nuclear capabilities remained peaceful, only for it to be rendered meaningless after the U.S. withdrew from it during President Donald Trump's first term. These attacks now create a new dynamic, wherein Iran is compelled to seek nuclear weapons by withdrawing from its commitments – its parliament is now mulling a bill to exit the NPT – and use them as a deterrent. Meanwhile, any step Iran takes to do so could be used to justify further aggression by Israel and the U.S., thereby rejecting international laws and the NPT's nonproliferation norm.

Israel's hypocrisy is stark. It remains a non-signatory to the NPT and refuses any oversight of its undeclared, but known, arsenal. This raises the possibility that it values nuclear weapons not for deterrence but for their destructive potential. U.S. protection emboldens it to pursue destructive policies in Gaza and illegal wars in West Asia. Combined with the Russian threat to use nuclear weapons to deter conventional aggression by NATO following its Ukraine invasion, these actions reveal how the renewed "competition among the great powers" and their cynical understanding of deterrence are dismantling global stability. The idea of nuclear disarmament is in tatters as the nuclear-weapon states continue to expand and modernise their arsenals, while non-proliferation is under threat as other countries turn to nuclear weapons to safeguard themselves. Without a renewed diplomatic impetus to re-establish international norms on conflict, a stronger push for disarmament among all nuclear-armed states, and a firm commitment to uphold the NPT, the world risks sliding into a new era of nuclear brinkmanship that could prove more dangerous than the Cold War's darkest moments.

A reset in West Asia, a 'de-escalation' for the world

West Asia has been reset with the bombing of Iran by Israel and the United States. It has been done with the tacit or open approval of almost all countries in the region and beyond. The Europeans have been their usual contradictory noisy self, but made no difference to what is unfolding in West Asia. Even Russia and China, which signed, with much fanfare, Comprehensive Strategic Partnership agreements with Iran in January 2025 and March 2021 respectively, were silent spectators. It is not that all these countries were helpless. They made a conscious decision not to interfere when Iran and its proxies are being dismantled in the region.

The reality now

Now with the so-called Iranian nuclear threat being rendered ineffective, West Asia is faced with a sole dominant nuclear power – Israel. The region has 40,000 American troops stationed on its soil in addition to numerous air and sea assets. They will make sure that there is no more military challenge to Israel. West Asia will now live with this reality.

Initially, the Gulf and other countries of West Asia feared, probably rightly, Iran and its proxies as much as the Israelis. The Iranian strategic and military depth in the region, when seen through the prism of its political ideology, made it the predominant threat in the region. In some ways, the presence of an aggressive Iran made the Gulf countries soft pedal, and even make compromises on many other issues which the region has been plagued with, including Palestine. They needed Israel and the U.S. to balance their vulnerability *vis-à-vis* Iran, which only encouraged Israel to go all the way out to dismantle the Iranian proxies, both state and non-state actors, in Lebanon, Syria and Gaza. The threat has receded except perhaps for the Houthis in Yemen and the militias in Iraq. In the meantime, the Gulf countries have been busy building bridges with the U.S. administration and waiting to operationalise Abraham Accords, which normalised their relations with Israel. They have made U.S. President Donald Trump happy by doling out goodies. But, with the cutting down of Iran to size in West Asia, do they relish the prospect of an Israel without any checks? Probably not. Can they do something at least now?

Iran has hit back. Its missiles have targeted U.S. military bases in Qatar – the biggest U.S. base in West Asia with 10,000 personnel, and in Iraq. Iran claimed proportional retaliation in that the number of missiles used was equal to the number of bombs the U.S. used to attack Iran's nuclear facilities. This represented a dangerous escalation, violating the territorial integrity of one of its own "brotherly" countries, Qatar, and with the situation threatening to spiral out of control. The retaliation was not entirely unexpected.

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While the U.S.'s announcement of a ceasefire between Israel and Iran is a surprising voice of reason, for the rest of the world, what matters is only 'de-escalation'

For Iran's leadership, it is an existential crisis. For the Supreme leader, Ayatollah Ali Khamenei, and the leadership, surrendering or keeping quiet in the face of these attacks are not options if they must survive politically.

They know that the end game is regime change to dismantle their theological foundation and political ideology – an ideology which threatens everyone in the region. To that extent, the war with Iran is still a work-in-progress for Israel and the U.S. They will not stop until they do a "Syria" on Iran. But there is no alternate "regime" waiting to take their place. Consequently, for their own good, the Gulf states need to step up now to prevent an Iraq- or a Libya-like collapse, which will destabilise everyone in the region. Destabilising regimes in the region has only given a fillip to Islamic fundamentalism and to terrorist organisations such as the Islamic State and al-Qaeda.

As one spat ends another crisis begins

The dramatic announcement by the U.S. of an immediate ceasefire between Israel and Iran is a surprising voice of reason, at a time when reason has become the biggest casualty in West Asia. After retaliation for the U.S. bombing and proving to the world – and more importantly to its people – that it will not be cowed down, the ceasefire call gives Iran a way out to back down. Let us not forget that Israel too has been hit hard though the western media has played it down. The fact that Iran was ready to hit American bases in the Gulf would have weighed on the U.S. to pressure Israel to stop.

It is also a wakeup call for the Gulf leadership that they are not immune. Hopefully, this should stop Iran from making good on other threats such as closing the Strait of Hormuz or exiting the Nuclear Non-Proliferation Treaty. The focus shifts back to the nuclear deal, where both the U.S. and Iran may well be in a mood to find a solution. It is time for the Gulf states to support this process, even if it is late, to save the region from further conflagration.

While this spat sputters to an end, the next crisis in West Asia is in the making. With the long-cherished dream of Israel's Prime Minister Benjamin Netanyahu realised under Mr. Trump – to take out Iran's nuclear programme – his domestic political fortunes have been revived dramatically. There are hardly any obstacles now for him to realise his "Eretz Israel" dream – the promised land from the Jordan river to the Mediterranean Sea. This is the New Middle East map which Mr. Netanyahu waved before the UN General Assembly to 193-member states – a map without Gaza or the West Bank. Israeli plans to annex them very soon and certainly before the U.S. presidential elections in 2026. If his main ultra-right coalition ministerial colleagues Itamar Ben-Gvir and Bezalel Smotrich are to be believed, and there is no reason why they should not be, this annexation will happen this year. All state and non-state actors, which can potentially oppose the move, have been defeated or chastised. The U.S. is also in sync with Mr. Netanyahu in his ambitions. The question will then boil down to these: After its annexation of Palestinian territories, will Israel continue to be an apartheid state by choice to preserve its Jewishness, where the Palestinians will not enjoy equal citizenship and remain second class citizens? Or it will become a genuine democracy by giving the Palestinians equal rights as its Jewish citizens. History indicates that it will be the first.

While the opposition to this annexation should come from countries within the region, the Gulf leadership has almost given up pushing Israel for a Palestinian state or even stopping the Gaza war as the price to pay for regional stability and integration with Israel and the outside world, their noisy protestations within and outside the UN notwithstanding. However, if they think that peace and security will be restored by annexing Palestinian territories or even status quo of occupation retained (56,000 Palestinians have been killed in Gaza, those displaced, face daily threats, starvation and displacement, while people in the West Bank are driven out of their homes to make way for Jewish settlers), they may be forced to rethink their strategy.

India's stand

Expectedly, India has neither made pronouncements on the Israeli preemptive strikes on Iran nor taken an active role – just as it has not in other wars elsewhere. Israel was one of few countries to stand by India during Operation Sindoor. However, India's joint initiatives with Iran, including Chabahar port connectivity, are equally important. India's stakes in the region are high and it is doing all it can to minimise the impact. India has, tongue in cheek, called for a "de-escalation", giving the same advice to warring parties which it received during Operation Sindoor from many parts of the world, asking India and Pakistan to de-escalate. It was a case of equating the aggressor and the aggressed. It matters no more to the world, whether one is right or wrong or whether international law or territorial integrity have been violated, as long as the warring sides "de-escalate".

Technique to make CAR T-cells in vivo could transform cancer care

CAR T-cell therapy retrains immune cells to recognise and destroy rogue targets. T cells often fail to identify cancer cells, so scientists insert genetic instructions that make them express the synthetic molecule, CAR. It gives T cells the ability to detect a specific 'tag' implicated in these cancers

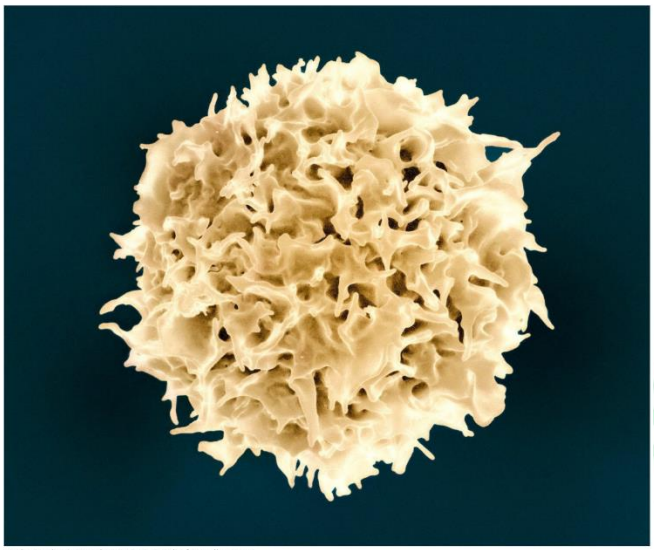
Anirban Mukhopadhyay

In recent years, chimeric antigen receptor (CAR) T-cell therapy has changed outcomes for patients with aggressive blood cancers that no longer respond to standard treatments. In some acute leukaemias, CAR T-cell therapy has led to remissions lasting months or even years. Early-stage trials have explored its use in severe autoimmune diseases like lupus as well, where it may help reset a misfiring immune system.

Originally developed in the early 1990s, the central idea behind CAR T-cell therapy is to retrain the body's own immune cells to recognise and destroy rogue targets. T cells, the patrolling white blood cells, often fail to identify cancer cells. So scientists extract a patient's T cells and insert genetic instructions that make them express the synthetic molecule, CAR. It gives T cells the ability to detect a specific 'tag' – most often CD19, which is found on nearly all B cells – that are the primary culprits in these cancers.

Once these reprogrammed T cells are infused back into the body, they expand, circulate, detect, and eliminate. The process is targeted and potent – but also slow, expensive, and complex. It requires personalised cell harvesting, lab-based genetic engineering using viral vectors, and chemotherapy to prepare the body to receive the modified cells.

Dr. Vishwanath S., a senior consultant in medical oncology, Apollo Hospitals, Bengaluru, estimated from personal practice that CAR T-cell therapy in India typically costs around ₹60-70 lakh. "Roughly ₹30-35 lakh goes toward manufacturing the personalised CAR T-cells through complex *ex vivo* processing," he said. "The rest covers hospitalisation, supportive care, and monitoring for two to three weeks – including side effects, infections, and post-infusion care."



A colourised scanning electron micrograph of a T cell. US NIAID

Engineering T-cells inside the body

A study in *Science* on June 19 by researchers from the US National Institute of Arthritis and Musculoskeletal and Skin Diseases, Capstan Therapeutics, and the University of Pennsylvania takes the core idea of CAR T-cell therapy and moves it entirely inside the body.

Instead of extracting T cells and engineering them in a lab, the researchers delivered messenger RNA directly into circulating immune cells using tiny, fat-based molecules known as lipid nanoparticles (LNPs). Commonly used in mRNA vaccines, they help genetic instructions enter target cells. To make sure the message reached the right cells, the researchers added a kind of biological address label: antibodies that bind specifically to CD8+ T cells, the immune system's frontline killers. This targeted formulation, called a CD8-targeted lipid nanoparticle (CD8-tLNP) allowed the instructions to be delivered with precision.

When injected into mice, tLNPs carrying instructions for a CD19-targeting CAR successfully reprogrammed circulating CD8+ T cells, while in cynomolgus monkeys, a CD20-targeting version was used. Within days, B cells were depleted across multiple tissues, and tumours regressed in mice – all without personalised cell processing, viral vectors or chemotherapy. In monkeys, the treatment turned most CD8+ T cells (up to 85%) and nearly all related immune cells (95%) into cancer fighters after the second or third dose, showing strong results.

Bypassing bottlenecks

The key advantage of this platform is that it avoids several of the most restrictive components of current CAR T-cell therapy, and without compromising function.

Since the CAR instructions were delivered using mRNA rather than viruses, the changes to the immune cells were temporary, lowering the risk of permanent genetic side effects. The therapy also worked without lymphodepleting chemotherapy – a preparatory treatment that wipes out a patient's existing immune cells to make space for the modified T cells. This step carries risks of serious secondary infections due to low immunoglobulin levels, necessitating prolonged and recurrent hospital admissions. And because the entire process took place inside the body, there was no need for custom lab-based cell manufacturing. Dr. Vishwanath noted that the ability to bypass both complex *in vitro* manufacturing and chemotherapy-based lymphodepletion could make CAR T-cell therapies safer and more accessible for frail, elderly, and comorbid patients.

The researchers also introduced a newly developed component, Lipid 829, a biodegradable carrier designed for improved tolerability. It showed faster clearance from the liver and lower inflammatory markers than earlier nanoparticle formulations while still delivering the CAR instructions effectively to T cells.

Signs of an immune reset

Beyond cancer, the study also explored whether the same platform could target B cells in autoimmune settings, where they mistakenly attack the body's own cells.

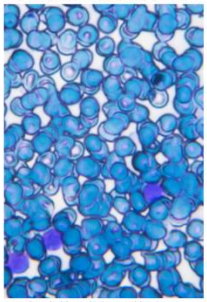
In monkeys, the treatment led to near-complete depletion of circulating and tissue-resident B cells, including in the spleen, lymph nodes, and bone marrow. Over the following weeks, fresh B cells gradually returned – and when they did, they were mostly naïve, like new recruits with no memory of having turned against their own body. This mirrored observations from human trials of conventional CAR T-cell therapy in lupus, where long-term remission has been linked to repopulation by naïve B cells.

The researchers also tested the platform on blood samples from patients with lupus and myositis. In laboratory assays, CD8-tLNPs successfully reprogrammed the patients' own T cells, which then eliminated their B cells *in vitro*.

While these findings remain preclinical, they reinforce that transient CAR expression might offer a way to reset the immune system without long-term immunosuppression.

What the safety data say

The risks associated with conventional CAR T-cell therapy include cytokine release syndrome (CRS), neurological complications, and, in some cases, long-term effects from random integration of viral vectors in the patient's genome.



Acute lymphoblastic leukaemia blood smear under light microscopy. GETTY IMAGES

A patient who received CAR T-cell therapy for primary mediastinal B-cell lymphoma at Tata Memorial Centre in June 2024 said it was her fourth line of treatment after three earlier regimens had failed.

"It finally put my cancer into remission," she said. "But recovery hasn't been simple. I stayed 27 days in the hospital because of sepsis. I've had pneumonia and still get secondary infections due to low immunoglobulin levels. Another friend is facing something similar. One of the others who had the treatment with us – she had leukaemia – passed away recently, possibly from the same. I'm better; cancer free, but I wouldn't say I have been able to get back to how life was before my diagnosis."

She does however call herself an outlier and that others have had easier recoveries.

The new study aimed to minimise some of these risks by using non-integrating mRNA and the new lipid nanoparticle.

In monkeys, the treatment was mostly safe. Inflammation markers rose slightly after infusion but normalised with standard premedication of antihistamines and corticosteroids. Liver side effects, a concern with nanoparticles, were minimal with Lipid 829.

However, one monkey developed a serious immune overreaction resembling hemophagocytic lymphohistiocytosis – a known CAR T-cell therapy risk – after the last infusion and had to be euthanised. While this was a single case, it underscored the importance of careful dosing and clinical monitoring.

Dosing like a drug

In monkeys, two or three intravenous infusions, spaced 72 hours apart, were enough to induce CAR expression in circulating CD8+ T cells and achieve near-complete depletion of B cells across multiple tissues.

Because the formulation was standardised, not patient-specific, and required only intravenous dosing, the procedure resembled a biologic drug infusion more than a cell therapy protocol. In principle, this delivery model could reduce the need for specialised infrastructure.

The platform represents one of the most developed *in vivo* CAR T-cell systems tested to date. It showed functional results in mice and non-human primates, used a defined dosing regimen, and included safety modifications such as enhanced CD8 targeting and premedication.

Dr. Vishwanath said, "Robust human trials will be essential to confirm safety, efficacy, and long-term outcomes". How the body will react to the engineered T cells and repeat dosing remain open questions as well.

The key advantage of this platform is that it avoids the most restrictive components of current CAR T-cell therapy. Since CAR instructions were delivered using mRNA rather than viruses, changes to immune cells were temporary, lowering the risk of genetic side effects

"Reproducibility will be another major issue," Pankaj Prasad, who has worked extensively in cell and gene therapy in India and Singapore, cautioned. "When pilot experiments are performed in the R&D lab by humans and when they are reproduced by automated machines, there is always variability. The small-scale results do not match with the automated machine-generated results and usually require another loop of standardisation."

The study lays the technical groundwork for translation, but the safety, efficacy, and scalability of this approach in humans remain to be established. If future trials succeed, it could expand the scope of CAR T-cell therapy beyond what current platforms allow.

Matters for India

India faces a high burden of B cell-driven cancers. Regional cancer registries show that diffuse large B-cell lymphoma (DLBCL) – one of the most aggressive types – makes up 34-60% of non-Hodgkin lymphoma cases, followed by follicular lymphoma. Acute lymphoblastic leukaemia is the most common cancer in Indian children accounting for 75% of all cases. All of these conditions are candidates for conventional CAR T-cell therapy.

India's burden of autoimmune disorders is also rising, with one study suggesting a 30% increase in prevalence since the COVID-19 pandemic.

The approach described in the new study avoids many of the constraints that have limited the therapy's use in India. If proven safe and effective in humans, it could be ideal for settings where specialised infrastructure is limited and patient volume is high. Furthermore, a simplified, infusion-based platform like this could make advanced immunotherapy more widely feasible, especially in places where few cell therapy units and trained specialists limit access.

If it passes all the quality checks, this platform could shift not just how we deliver CAR T-cell therapy but also who can benefit from it.

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For first time, India breaks into top 100 in global SDG rankings

The index measures overall progress toward achieving the 17 Sustainable Development Goals adopted in 2015; India takes 99th rank, up from 109

Press Trust of India
NEW DELHI

India has, for the first time, secured a position among the top 100 countries in the Sustainable Development Goals (SDG) Index, ranking 99th out of 167 nations in the 2025 edition of the Sustainable Development Report (SDR), released on Tuesday by the UN Sustainable Development Solutions Network.

The latest report places India with a score of 67 on the SDG Index, a significant improvement from its 109th rank in 2024. China is ranked 49th with a score of 74.4, while the United States stands at 44th with 75.2 points.

The index measures overall progress toward achieving the 17 SDGs adopted by United Nations member states in 2015, with a score of 100 indicating full achievement of all goals.

Among India's neighbours, Bhutan ranks 74th (70.5), Nepal 85th (68.6), Bangladesh 114th (63.9), and Pakistan 140th (57). Maritime neighbours Maldives and Sri Lanka stand at 53rd and 93rd places respectively.

The report noted that since the adoption of the SDGs, India has steadily improved its standing: it ranked 112th in 2023, 121st in 2022, and 120th in 2021.

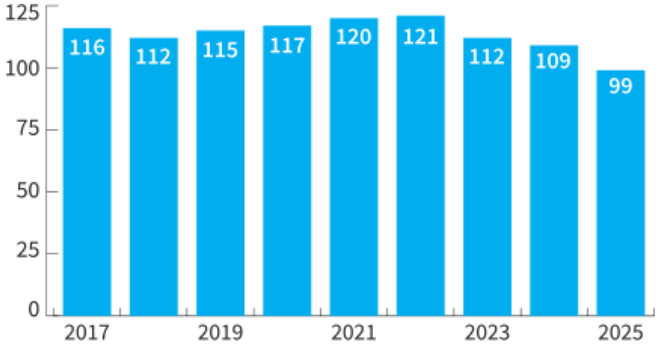
Despite India's gains, the report flagged that global progress on the SDGs has largely stalled. "Only 17 per cent of the SDG targets are on track to be achieved by 2030," it stated, attributing this to "conflicts, structural vulnerabilities, and limited fiscal space" in many regions.

The SDR, authored by a team led by economist Jeffrey Sachs, pointed to continued dominance by European nations on the index. Finland, Sweden and Denmark hold the top three positions, with 19 of the top 20 countries located in Europe.

However, even these nations are facing challenges related to climate change and biodiversity due to unsustainable consumption patterns.

Moving up

India ranks 99th on the 2025 SDG Index with a score of 67, while China ranks 49th with 74.4 and the US 44th with 75.2 points



SOURCE: UNSD

‘Operation Sindoor showed India’s uncompromising anti-terror policy’

The Hindu Bureau
NEW DELHI

Operation Sindoor clearly demonstrated India’s firm and uncompromising policy against terrorism on the global stage, Prime Minister Narendra Modi said on Tuesday, affirming that no shelter was safe for terrorists who spilt the blood of Indian citizens.

“Today’s India takes decisions based solely on what is right for national interest,” Mr. Modi said, adding that India’s dependence on foreign nations for military needs is steadily decreasing as the country is becoming self-reliant in the defence sector.

The Prime Minister noted that this shift was evident during Operation Sindoor, where the armed forces forced the “enemy into surrendering within 22 minutes using domestically manufactured weapons”. In the days ahead, “Made-in-India” weapons will earn global recognition and acclaim, he said.

Prime Minister Narendra Modi offers a floral tribute to Sree Narayana Guru in New Delhi on Tuesday. PMO

Historic conversation

He was speaking at an event marking the centenary celebration of the conversation between Sree Narayana Guru and Mahatma Gandhi at Sivagiri Math in Varkala, Kerala, on March 12, 1925. The meeting “remains inspirational and relevant even today, and serves as a powerful source of energy for social harmony and for collective goals of a developed India,” Mr. Modi said. “The ideals of Sree Narayana Guru are a great asset to all of humanity,” he added.

‘Mantra of unity’

His mantra – “*Oru Jati, Oru Matham, Oru Daivam, Manushyanum* [One caste, one religion, one God for mankind]” – reflected the unity of all humanity and all living beings, a philosophy that formed the foundation of India’s civilisational ethos, he said.

“Sree Narayana Guru envisioned a society free from discrimination, Today, the country is eliminating every possibility of discrimination by following a saturation approach,” the Prime Minister said, highlighting his government’s welfare programmes to benefit millions of poor people, Dalits, tribals, and women.

15th-century lamp discovered in Karnataka temple

The Hindu Bureau
MANGALURU

An antique lamp, believed to be from the 15th century, with very rare Shaiva and Vaishnavaite sculpture carvings, has been discovered in the Anantapadmanabha temple at Perduru in the Udupi district of Karnataka.

"It is a rare blend of Shiva and Vishnu, and reflects the daily rituals of both the cults in the temple," said T. Murugeshi, a retired Associate Professor of ancient history and archaeology, Mulki Sunder Ram Shetty College, Shirva, Udupi.

The lamp was donated by Basavannaras Banga to the temple in 1456 CE. This is mentioned in a stone inscription in the inner *prakara* of the temple. "With this epigraphical reference, it is very clear that the lamp belongs to the 15th century," the historian said on Tuesday.

The antique lamp with rare Shaiva and Vaishnavaite sculptures found at the Anantapadmanabha temple in Udupi. The other side of the lamp shows Brahma holding a sacred book.

"This single piece of lamp has two faces, and has narrative sculptures of a *Puranic* story. On the first face, Lord Shiva is seen in a dancing pose as Nataraja with four hands. On his left is a man beating a drum. To the drummer's left is Parvati seated on a bull, and Ganapati on his vehicle (rat). On the right side of Nataraja, the Bringi playing tala is seen. Khadga Ravana seated on a woman (Goddess Mari) is also seen. On his right, Kumara is seated on a peacock," the historian said.

"This depiction very clearly narrates the story of *the Pralya Tandav*a (destructive dance) of Lord Shiva," Mr. Murugeshi said.

"On the second face of the lamp, from the right side, Brahma is shown holding a sacred book in his left hand, and his right hand is in '*abhaya mudra*'. Next is Indra holding the '*vajra*' in his left hand. But the content of his right hand is unclear. At the centre, Anantapadmanabha is standing with four hands. Very interestingly, he holds *Uddarane* (spoon) and *shanka* (conch). On his left, Agni holds fire in his right hand, and Varuna holds conch in his left hand," Mr. Murugeshi pointed out.

Different headgear

"All five figures are seen in '*Samabhanga*' pose and have different headgear. It narrates that the gods, out of fear (because of the destructive dance of Lord Shiva), went to Vaikunta, the abode of Narayana, and prayed for the protection of the three worlds. Lord Anantapadmanabha, the protector of the three worlds, makes Lord Shiva calm. At the centre of the lamp's round base, Garuda is depicted in a standing pose. Behind, Lord Shiva is seen seated in *Anjalimudre* in a calm and peaceful posture and prays to Lord Anantapadmanabha," he said.

Find ways of increasing revenue of panchayats, Amit Shah urges CMs

States must strive to eradicate malnutrition, cut school dropout rate, says Union Home Minister at Zonal Council meeting in Varanasi; issues such as implementation of fast-track courts discussed

The Hindu Bureau
NEW DELHI

Union Minister for Home Affairs Amit Shah on Tuesday urged the Chief Ministers of four States – Uttarakhand, Uttar Pradesh, Chhattisgarh, and Madhya Pradesh – to devise ways and formulate rules to increase the revenue of gram panchayats. The BJP is in power in these States.

Mr. Shah said that enhancing the revenue of panchayats would make India's three-tier Panchayati Raj system more effective, according to a statement by the Ministry of Home Affairs.

The Union Minister made the comments while chairing the 25th Central Zonal Council meeting in Varanasi, which was attended by U.P. CM Yogi Adityanath, Uttarakhand CM Pushkar Singh Dhami, Madhya Pradesh CM Mohan Yadav, and Chhattisgarh CM Vishnu Deo Sai.

Nineteen issues were discussed, including several matters of national importance, the MHA said.

Union Home Minister Amit Shah with Uttar Pradesh Chief Minister Yogi Adityanath in Varanasi, U.P., on Tuesday. ANI

The implementation of fast track special courts for speedy investigation and prompt disposal of cases of rape involving women and children; brick and mortar banking facilities in every village; and execution of the Emergency Response Support System were among the key issues discussed at the meeting.

Mr. Shah said that all States must work towards eradicating child malnutrition, reducing the school dropout ratio to zero, and strengthening the cooperative sector.

'Twofold rise in meets'

He also said that only 11 Zonal Council meetings and 14 meetings of the Standing Committees were held between 2004 and 2014. However, the period from 2014 to 2025 saw a twofold increase, with 28 Zonal Council meetings and 33 meetings of the Standing Committees.

Following their discussion, the CMs issued posts on X, sharing highlights of the meeting.

Mr. Dhami said, "During the meeting, I requested increased support through the Border Roads Organisation to strengthen road, communication, and security infrastructure in the border areas."

Meeting ground

Mr. Adityanath and Mr. Sai said the council "strengthens federal unity, national integrity, and regional development".

Five Zonal Councils were created under the States Reorganisation Act 1956 to provide a common meeting ground for States and Union territories to resolve inter-State and regional issues.

The Union Home Minister chairs all the councils, with CMs, Lieutenant-Governors or administrators of member States and UTs as members.

(with inputs from PTI)