STEM CELLS & EXOSOMES

# Do stem cell infusions or exosomes slow systemic ageing in humans?

Separating tightly regulated cellular engraftment trials from off-the-shelf mesenchymal signalling infusions and extracellular vesicles.

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Over 80% of intravenously infused mesenchymal stem cells trap in the pulmonary capillary bed within minutes and clear from the body within 72 hours, meaning any systemic effect relies on brief chemical signalling rather than permanent tissue replacement.

Search interest in regenerative medicine frequently merges two fundamentally distinct biological interventions under the single label of stem cell therapy. On one side are highly regulated, lineage-specific cellular transplants—such as autologous induced pluripotent stem cell (iPSC)-derived dopaminergic progenitors surgically implanted into the putamen for neurodegenerative movement disorders. On the other side are cash-pay intravenous infusions of allogeneic mesenchymal stromal cells (MSCs) or acellular exosome preparations marketed to healthy adults for systemic anti-ageing. Understanding the biological boundary between structural cell engraftment and transient paracrine immunomodulation is essential for evaluating clinical trial headlines and assessing the real-world risks and utility of regenerative biologics.

## What it is

The umbrella term 'stem cell therapy' covers multiple distinct biological entities that share very little in mechanism, manufacturing, or clinical intent. Induced Pluripotent Stem Cells (iPSCs) and Lineage-Specific Progenitors Adult somatic cells (such as skin fibroblasts or peripheral blood mononuclear cells) can be reprogrammed back into an embryonic-like pluripotent state by introducing specific transcription factors (Oct4, Sox2, Klf4, and c-Myc, collectively known as Yamanaka factors). Once reprogrammed, these iPSCs can be directed in a laboratory to differentiate into specific cell types—such as retinal pigment epithelium, cardiac myocytes, or A9 dopaminergic neuron progenitors. When derived from the patient's own cells (autologous), they minimize immune rejection. In investigative guides—such as early Phase 1 data for UX-DA001 presented at neurological movement disorder congresses—these differentiated progenitor cells are delivered directly into the target tissue via stereotactic neurosurgery to replace lost functional neurons and reconstruct local circuitry. Mesenchymal Stromal Cells (MSCs) Commercial clinics rarely use iPSCs due to the complexity of directed differentiation and the risk of teratoma (tumour) formation from residual undifferentiated cells. Instead, they rely on mesenchymal stem cells—more accurately termed mesenchymal stromal cells or medicinal signalling cells. These multipotent cells are harvested from adult bone marrow, adipose (fat) tissue, or perinatal birth tissues (umbilical cord Wharton's jelly, placenta). In culture, they express surface markers CD73, CD90, and CD105 while lacking hematopoietic markers CD14, CD34, CD45, and HLA-DR. Despite their name, intravenously infused MSCs do not travel to ageing organs and differentiate into new heart, liver, or brain tissue. Exosomes and Extracellular Vesicles (EVs) Exosomes are a subset of lipid-bilayer extracellular vesicles measuring 30 to 150 nanometres in diameter. They are formed inside the cell within multivesicular bodies and released into the extracellular space when these bodies fuse with the plasma membrane, carrying surface tetraspanin markers CD9, CD63, and CD81. Exosomes are acellular; they cannot divide or engraft. They function as biological

shipping containers, transferring proteins, lipids, messenger RNAs (mRNAs), and non-coding microRNAs (miRNAs) from a donor cell to a recipient cell. Because MSCs exert most of their effects through secreted factors rather than physical engraftment, commercial operators have shifted toward isolating the secretome or exosomes from cultured MSCs to offer an off-the-shelf, cell-free product.

## Why it is used

In evidence-based medicine, true cellular replacement therapies are investigated to restore lost anatomical structure and physiological function in severe degenerative or hematological diseases. Hematopoietic stem cell transplantation (HSCT) is the standard of care for reconstituting bone marrow after myeloablative chemotherapy in leukemias and lymphomas. In regenerative neurology and ophthalmology, investigational iPSC and embryonic stem cell guides aim to physically replace discrete populations of dead cells—such as striatal dopamine neurons in Parkinson disease or photoreceptor-supporting cells in macular degeneration. In the cash-pay longevity and sports medicine sector, MSCs and exosomes are used for entirely different reasons: immunomodulation, suppression of chronic low-grade inflammation ('inflammaging'), and local tissue trophic support. Ageing is accompanied by an accumulation of senescent cells that secrete pro-inflammatory cytokines, chemokines, and matrix-degrading proteases—known as the Senescence-Associated Secretory Phenotype (SASP). Systemically, individuals pursue intravenous MSC or exosome infusions with the goal of downregulating this inflammatory milieu, improving endothelial function, and enhancing recovery. Locally, intra-articular injections of autologous bone marrow aspirate concentrate (BMAC), stromal vascular fraction (SVF), or cultured MSCs are used to manage pain and functional decline in knee or hip osteoarthritis, or to accelerate tendon and ligament healing without surgery.

## How it helps

The mechanisms of action depend entirely on the product class and route of administration, and must be separated into what is established in humans versus what remains confined to cell culture and rodent models. Paracrine Signalling and the Pulmonary First-Pass Effect (Human & Preclinical Evidence) Radiolabelling and bioluminescence tracking studies in both rodents and humans demonstrate that when MSCs are infused via a peripheral vein, 80% to 90% are physically trapped in the microvasculature of the lungs within minutes due to cell size (typically 15 to 30 micrometres in culture) and endothelial adhesion molecules (such as VCAM-1 and VLA-4). Most trapped cells undergo apoptosis (programmed cell death) within 24 to 72 hours. However, this rapid death is now understood in human immunology to be a primary mechanism of action, termed efferocytosis. Alveolar and splenic macrophages engulf the apoptotic MSCs, which triggers a phenotypic switch in the host macrophages from a pro-inflammatory M1 state to an anti-inflammatory, tissue-repairing M2 state. Before and during clearance, MSCs respond to host inflammatory signals (such as IFN-gamma and TNF-alpha) by secreting anti-inflammatory cytokines and growth factors, including Interleukin-10 (IL-10), Transforming Growth Factor-beta (TGF-beta), Prostaglandin E2 (PGE2), Indoleamine 2,3-dioxygenase (IDO), Hepatocyte Growth Factor (HGF), and Vascular Endothelial Growth Factor (VEGF). These factors suppress T-cell proliferation, promote regulatory T-cells (Tregs), and inhibit dendritic cell maturation. Exosome Cargo Transfer (Primarily Preclinical Evidence) Exosomes bypass pulmonary capillary trapping to a greater degree than whole cells due to their nanometer scale, though pharmacokinetic studies in animals show they are primarily cleared by the reticuloendothelial system in the liver and spleen within hours. In cell culture and rodent injury models, MSC-derived exosomes transfer specific microRNAs to recipient cells. For example, miR-21, miR-146a, and miR-181c have been shown in vitro and in mice to inhibit the Toll-like receptor 4 (TLR4) and Nuclear Factor kappa B (NF-kB) inflammatory cascade, while activating the PI3K/Akt and Wnt/beta-catenin pathways to promote cell survival and angiogenesis. Whether commercial exosome vials contain sufficient concentrations of intact, biologically active miRNA to alter gene expression in adult human tissues after systemic dilution remains

unproven in human trials. Evidence Quality and Effect Sizes For systemic ageing, human evidence is limited to small Phase 1 and Phase 2 trials investigating physical frailty in older adults (mean age typically 75 to 78 years). In randomized controlled trials of allogeneic bone marrow-derived MSCs (such as the CRATUS trial series, enrolling 30 to 36 participants followed for 6 to 12 months), single intravenous infusions of 100 million cells improved 6-minute walk distance by approximately 35 to 40 metres and reduced serum TNF-alpha levels compared to starting point, whereas higher doses (200 million cells) paradoxically showed weaker clinical responses. No reliable effect size exists for lifespan extension, epigenetic age reversal, or disease prevention in healthy adults aged 40 to 65. For knee osteoarthritis, meta-analyses of randomized controlled trials (enrolling several hundred patients across studies lasting 6 to 24 months) show that intra-articular MSC injections reduce pain scores on the Visual Analogue Scale (VAS) by roughly 15 to 25 mm (on a 100 mm scale) and improve WOMAC functional scores compared to saline or hyaluronic acid. However, sequential magnetic resonance imaging (MRI) rarely demonstrates clinically meaningful regeneration of hyaline cartilage volume. Non-Obvious Synthesis: Why Symptom Scores Move While Tissue Structure Does Not A recurring paradox in regenerative medicine is that patients receiving intra-articular MSCs or systemic biologics report rapid reductions in joint pain or systemic fatigue, yet structural imaging (such as T2-mapping MRI of articular cartilage) or long-term functional organ metrics remain unchanged. Similarly, in systemic frailty trials, circulating TNF-alpha drops without consistent gains in skeletal muscle mass or grip strength. This disconnect occurs because the intervention acts as a transient biological anti-inflammatory—driven by PGE2, IL-10, and macrophage efferocytosis—rather than a structural tissue builder. Suppressing synovial inflammation quiets nociceptive pain fibres in a joint just as a corticosteroid does, creating genuine symptomatic relief that patients and clinicians frequently misinterpret as structural tissue regeneration. Conversely, when structural regeneration actually occurs—as seen in early Phase 1 surgical trials of autologous iPSC progenitors for Parkinson disease—the clinical motor improvements develop slowly over 6 to 18 months as engrafted neurons mature and form synaptic connections, bearing no resemblance to the rapid anti-inflammatory effect of a wellness clinic drip.

## Who should try it

Outside of standard-of-care hematological transplants and approved tissue-engineered products for specific surgical defects, cellular and exosome therapies should primarily be accessed within registered, institutional review board (IRB)-supervised clinical trials. Candidates for Local Investigational or Orthopaedic guides Adults aged 40 to 65 with mild-to-moderate osteoarthritis (Kellgren-Lawrence grades 2 to 3) or chronic tendinopathies who have failed conservative physical therapy, weight management, and standard intra-articular injections may consider autologous orthobiologics (such as leukocyte-poor platelet-rich plasma or bone marrow aspirate concentrate) administered by qualified sports medicine physicians using ultrasound or fluoroscopic guidance. Here, the goal is local symptom modulation and functional physical therapy progression, not guaranteed joint regeneration. Who Should Avoid Commercial Systemic Infusions Healthy individuals seeking primary prevention of ageing should avoid cash-pay intravenous MSC or exosome infusions. The biological rationale does not support permanent tissue renewal from intravenous delivery, and no clinical trial data exist demonstrating long-term healthspan benefits in non-frail middle-aged adults. Contraindications and Trade-offs Active or recent history of malignancy is a strict contraindication for both MSCs and exosomes. Because MSC secretomes and exosomes carry angiogenic growth factors (like VEGF) and anti-apoptotic microRNAs while suppressing local T-cell surveillance, they can theoretically promote the vascularization and growth of occult tumours—a phenomenon documented in multiple preclinical oncology models. Other major trade-offs include: - Immunogenicity: While autologous cells avoid donor rejection, allogeneic (donor-derived) umbilical cord or placental MSCs are 'immune-evasive' rather than completely immune-privileged. Repeated infusions can induce donor-specific antibodies (HLA sensitization). - Infection and Contamination: Unregulated exosome and umbilical cord blood products have triggered severe adverse events, including polymicrobial sepsis (Escherichia coli, Enterococcus faecalis), viral transmission, and pyrogenic endotoxin reactions due to poor sterile

manufacturing practices. - Thromboembolism: Intravenous MSCs express Tissue Factor (CD142) on their surface, which can trigger the coagulation cascade upon contact with blood (the instant blood-mediated inflammatory reaction, or IBMIR), carrying a documented risk of pulmonary embolism or deep vein thrombosis. - Cost and Opportunity Cost: Out-of-pocket costs for systemic infusions typically range from $5,000 to $25,000 per session. Because paracrine effects dissipate within weeks to months, clinics often recommend repeat dosing, diverting substantial capital and attention from high-evidence interventions that directly remodel ageing physiology, such as structured cardiorespiratory training, resistance exercise, and lipid and glycemic control.

## Measurements that show improvement

If an individual participates in a clinical trial or undergoes an orthobiologic procedure, objective tracking separates true physiological shifts from placebo responses and regression to the mean. A physician-led longevity platform or clinical team will typically monitor a combination of inflammatory biomarkers, functional metrics, and structural imaging. Systemic Inflammatory and Immune Markers (for intravenous guides) - High-sensitivity C-Reactive Protein (hs-CRP): A hepatic acute-phase reactant driven by IL-6. A meaningful anti-inflammatory shift involves a sustained reduction toward <1.0 mg/L in individuals with elevated starting point systemic inflammation. - Pro-inflammatory Cytokine Panels (TNF-alpha, IL-6, IL-1beta): Research-grade or specialized clinical assays tracking reductions in circulating SASP components over 30 to 90 days post-infusion. - Lymphocyte Subsets: Flow cytometry assessing the ratio of regulatory T-cells (CD4+CD25+FoxP3+) to effector T-cells, reflecting systemic immunomodulation. Physiological and Composite Ageing Markers - Heart Rate Variability (HRV) and Resting Heart Rate (RHR): An acute drop in HRV and spike in RHR in the 24 to 72 hours following an infusion indicates an acute febrile or immune-clearance reaction, whereas long-term upward trends in root mean square of successive differences (RMSSD) reflect improved autonomic balance. - VO2max and 6-Minute Walk Distance: Objective cardiorespiratory and functional capacity metrics. In clinical frailty studies, a gain of >30 metres in 6-minute walk distance is considered clinically meaningful. - Grip Strength: Measured via handheld dynamometry (in kilograms), tracking whether systemic inflammation reduction translates into preserved neuromuscular function. - Composite Biological Age (BioAge) and Epigenetic Clocks: Multi-system blood biomarker composites (incorporating albumin, creatinine, glucose, alkaline phosphatase, mean corpuscular volume, red cell distribution width, lymphocyte percentage, and hs-CRP) or DNA methylation algorithms (such as DunedinPACE or GrimAge). Note that transient shifts in white blood cell subsets after an infusion can artificially skew blood-based epigenetic clocks without reflecting true tissue rejuvenation. Local Structural and Functional Markers (for orthopaedic guides) - Validated Patient-Reported Outcomes: WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) or KOOS (Knee Injury and Osteoarthritis Outcome Score), looking for >20% improvement at 3, 6, and 12 months. - Quantitative Joint MRI (T2 Mapping or dGEMRIC): Evaluates proteoglycan content and collagen fibre orientation in articular cartilage at 12 months post-injection to verify whether structural preservation occurred alongside pain relief.

## Products and services

These LetsGo products and services sit next to this subject. They are not a prescription. A link is not evidence that the product causes the change discussed above. - [LetsGo Academy](/academy) — The teaching track for coaches who use these explainers with members. - [LetsGo programmes](/programs) — Coached programmes. Not a clinic menu and not a promise of a result.

## Practical takeaways

- Distinguish product classes immediately: surgical engraftment of differentiated iPSCs for severe organ or neurological disease has no biological overlap with intravenous mesenchymal stem cell or exosome wellness drips.

• Verify regulatory status before consenting to any biologic: ask for the specific Investigational New Drug (IND) application number and Institutional Review Board (IRB) guide if a clinic claims to be running a clinical study.
• Never accept intravenous exosome or allogeneic cell infusions if you have an active malignancy, a history of hormone-sensitive or solid-organ cancer, or a predisposition to blood clots (thrombophilia).
• If pursuing local orthobiologics for joint osteoarthritis, prioritize autologous preparations (such as leukocyte-poor PRP or bone marrow aspirate concentrate) delivered under ultrasound guidance alongside a structured mechanical loading and physical therapy program.
• Use objective pre- and post-intervention biomarkers—such as hs-CRP, WOMAC functional scores, and quantitative MRI at 6 to 12 months—rather than relying on subjective short-term pain relief, which often reflects transient anti-inflammatory signalling rather than tissue regeneration.

## Safety note

Unapproved intravenous stem cell and exosome infusions carry documented risks of severe bacterial infection, endotoxic shock, pulmonary embolism (via Tissue Factor-mediated coagulation), donor HLA sensitization, and theoretical promotion of occult malignancies through angiogenic signalling. Any acute post-infusion fever, chills, chest pain, or shortness of breath requires immediate emergency medical evaluation.

## Disclaimer

This article is for educational and informational purposes only and does not constitute medical advice, diagnosis, or treatment. Stem cell and exosome therapies outside of approved hematological and specific tissue indications remain investigational. Always consult a qualified, licensed physician before making decisions regarding regenerative biologics or clinical trial participation.

Cellular and vesicular biologics represent a rapidly advancing frontier in medical science, but their clinical reality requires strict separation by mechanism and indication. While autologous iPSC-derived progenitor transplants show genuine promise for surgically rebuilding discrete cellular populations in conditions like Parkinson disease, commercial intravenous mesenchymal stem cell and exosome infusions do not rebuild aged organs. Instead, systemic infusions act as short-lived, high-cost biological anti-inflammatories mediated by pulmonary trapping and macrophage clearance. For adults aged 40 to 65, tracking objective inflammatory and functional markers while prioritizing proven physiological inputs remains the foundation of longevity medicine until standardized, rigorously tested regenerative guides complete human clinical trials.