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NAD^+ Precursors In Surgery And Hair Transplantation: A Narrative Review Of Mechanisms, Evidence And Translational Opportunities

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Abstract
Background:
Nicotinamide adenine dinucleotide (NAD^+) is a central redox cofactor and signalling molecule that regulates energy metabolism, DNA repair, sirtuin activity, inflammation and stem-cell function.
Ageing, metabolic disease and chronic stress are associated with a decline in NAD^+, which may impair tissue resilience and wound healing—key determinants of surgical outcomes. NAD^+ precursor supplementation with nicotinamide (NAM), nicotinamide riboside (NR), nicotinamide mononucleotide (NMN) and related compounds has emerged as a promising strategy to restore NAD^+ and improve organ function in preclinical and early clinical studies.
Objective:
To review the biological rationale and current evidence for the use of NAD^+ precursors in surgery in general, and to explore specific implications for hair transplant surgery and peri-follicular regeneration.
Methods:
A narrative review of the literature was performed using PubMed and major indexing services up to December 2025, focusing on NAD^+ biology, NAD^+ precursors (NR, NMN, NAM), regenerative medicine, wound healing, ischemia–reperfusion injury, skin and hair biology, and hair growth outcomes. Both preclinical and clinical studies were included.
Results:
Preclinical models demonstrate that NAD^+ repletion via NR, NMN or NAM improves mitochondrial function, reduces oxidative stress, enhances endothelial progenitor cell activity, accelerates wound closure and improves survival in models of cardiac arrest, ischemia–reperfusion, radiation injury, sepsis and diabetic wounds (1). In skin, NAD^+ restoration reduces cellular senescence and promotes keratinocyte proliferation and dermal regeneration (2). Hair-follicle biology is tightly linked to mitochondrial health; NMN has been shown to promote dermal papilla cell proliferation and hair growth in preclinical systems (3), while a first human clinical trial suggests that oral NMN can improve hair quality and subjective appearance in middle-aged women. (4) However, data specific to surgical patients and especially to hair transplant surgery remain limited, with no randomized controlled trials directly assessing perioperative NAD^+ precursors in this setting.
Conclusions:
Existing evidence supports a biologically plausible and increasingly well-documented role for NAD^+ precursors in enhancing tissue resilience, wound healing and organ protection in surgical and regenerative contexts. For hair transplantation, NAD^+ precursors represent a rational adjunct aimed at improving follicular stem-cell function, peri-follicular regeneration and donor/recipient healing, but dedicated clinical trials are urgently needed. Until such data are available, clinicians should regard NAD^+ precursor use in surgery and hair transplantation as a promising, largely extrapolated, adjunct—best employed within ethically designed protocols, with attention to safety, dosing and patient selection.

Keywords: *NAD^+; nicotinamide riboside; nicotinamide mononucleotide; nicotinamide; surgery; ischemia–reperfusion; wound healing; regenerative medicine; hair follicle; hair transplant; biological age; mitochondria.*

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I. Introduction

Surgical outcomes are traditionally framed in terms of technical skill, perioperative care and patient-specific risk factors such as age, comorbidity and smoking. Increasingly, however, these variables are being

understood through the lens of cellular bioenergetics and biological age rather than chronological age alone.

Nicotinamide adenine dinucleotide (NAD^+) is a central cofactor in mitochondrial oxidative phosphorylation and glycolysis, and a substrate for sirtuins, poly(ADP-ribose) polymerases (PARPs) and CD38. Through these pathways, NAD^+ influences DNA repair, redox balance, inflammation, stem- cell function and cellular senescence—processes that are critical for wound healing and tissue recovery after surgery (5).

With ageing and chronic disease, intracellular NAD^+ levels decline significantly, contributing to mitochondrial dysfunction, impaired stress responses and accelerated tissue ageing (6). NAD^+ precursor supplementation using nicotinamide (NAM), nicotinic acid (NA), nicotinamide riboside (NR) and nicotinamide mononucleotide (NMN) has been shown to restore NAD^+ levels and improve function across multiple organs in preclinical models; early human data suggest favourable safety and metabolic effects (7).

In parallel, hair biology has become a focus of regenerative medicine. Hair follicles are highly metabolic mini-organs undergoing cyclic phases of growth (anagen), regression (catagen) and rest (telogen), and are particularly sensitive to mitochondrial and redox status (8). Hair transplant surgery imposes additional metabolic challenges—ischemic intervals, microtrauma and reparative demands in the donor and recipient areas. Optimizing NAD^+ availability peri-operatively is therefore an attractive, though still largely theoretical, adjunct to improve graft survival and regeneration.

This review summarizes the biology of NAD^+ and its precursors, synthesizes the current evidence for their use in regenerative medicine and surgery, and discusses translational implications with a specific focus on hair transplant surgery.

II. Methods (Search Strategy And Selection Criteria)

Because the field is rapidly evolving, we conducted a narrative review rather than a formal systematic meta-analysis.

Databases searched: PubMed/MEDLINE, Google Scholar and major journal sites (e.g. Circulation, Plastic and Reconstructive Surgery, Redox Biology, Cells, Cosmetics) up to December 2025.

Search terms: “NAD+”, “nicotinamide riboside”, “nicotinamide mononucleotide”, “nicotinamide”, “NR”, “NMN”, “NAD precursor”, combined with “surgery”, “ischemia reperfusion”, “wound healing”, “skin”, “regenerative medicine”, “hair follicle”, “hair growth”, “alopecia”, and “hair transplantation”.

Inclusion criteria: Preclinical in vitro or in vivo studies and clinical trials or observational studies examining NAD^+ precursors in relation to organ protection, wound healing, skin or hair outcomes.

Exclusion criteria: Studies focused solely on non-surgical metabolic diseases without regenerative or tissue-injury endpoints; non-English abstracts when translation was not available.

Given the breadth of the NAD^+ literature, the cited studies are representative rather than exhaustive.

III. Biology Of NAD^+ And NAD^+ Precursors

NAD^+ functions both as a redox couple (NAD^+/NADH) and as a substrate for NAD-consuming enzymes. Sirtuins (SIRT1–7) regulate chromatin structure, mitochondrial biogenesis and cellular stress responses; PARPs facilitate DNA repair, while CD38/CD157 regulate calcium signalling and NAD^+ turnover (9).

NAD^+ pools decline with age due to:

Increased consumption by PARPs and CD38 in response to DNA damage and inflammation; Reduced salvage pathway activity;

Mitochondrial dysfunction and oxidative stress (10).

NAD^+ precursors include:

Nicotinamide (NAM) – classical vitamin B3 form, converted via the salvage pathway; Nicotinic acid (NA) – converted through the Preiss–Handler pathway;

Nicotinamide riboside (NR) – converted to NMN by NR kinases, then to NAD^+; (11)

Nicotinamide mononucleotide (NMN) – a direct precursor converted to NAD^+ by NMN adenylyltransferases (12);

Tryptophan – via the de novo kynurenine pathway.

Both NR and NMN have been shown to efficiently increase tissue NAD^+ in rodents and humans, with beneficial effects in cardiometabolic disease, neurodegeneration and ageing models (13).

IV. NAD⁺ Precursors And Perioperative Organ Protection

Cardiovascular and Ischemia–Reperfusion Injury

Several preclinical and early clinical studies support a protective role of NAD^+ precursors in ischemia–reperfusion injury—highly relevant to surgery and anaesthesia.

Cardiac arrest / global ischemia: Nicotinamide administration rapidly restored myocardial NAD^+, enhanced ATP and lactate production, and improved contractile recovery and survival in a mouse model of cardiac arrest (14).

Cardiac ischemia–reperfusion in humans: An observational study in patients receiving nicotinamide riboside suggested reduced cardiac ischemia–reperfusion injury in those also treated with certain anesthetic and antiplatelet regimens, supporting cardioprotective potential in clinical settings (15).

Vascular and endothelial health: A broader review of NAD^+ metabolism in cardiac health highlights that NAD^+-increasing strategies improve endothelial function, cardiac remodelling and resilience to stress in multiple animal models (16).

From a perioperative standpoint, these data suggest that pre-operative restoration of NAD^+ could improve tolerance to ischemia, reduce myocardial injury, and enhance recovery in high-risk cardiac and major non-cardiac surgery. Formal randomized trials are, however, still lacking.

Sepsis, Radiation, and Other Injury Models

Beyond classic surgical IR injury, NR and related precursors have shown protective effects in other severe tissue-injury models:

Sepsis and ovarian injury: NR reduced ovarian inflammation and structural damage in a sepsis model (17).

Spinal cord injury: NR enhanced tissue preservation and functional recovery in experimental spinal cord injury (18).

Radiation-induced intestinal senescence: NR attenuated radiation-induced intestinal ageing and functional decline (19).

These findings complement the cardiovascular data, suggesting a generalizable pattern of NAD^+- linked protection across diverse tissues and insults relevant to perioperative medicine.

Caveats and Context

Notably, one recent study reported that long-term NAD^+ precursor supplementation could, under specific conditions, sensitize the brain to subsequent ischemic events despite showing neuroprotective effects with acute dosing (20). This underlines the importance of context (tissue, timing, dose, and duration) and cautions against assuming uniform benefit across all clinical scenarios.

V. NAD⁺, Wound Healing And Skin Regeneration

Skin and surgical wounds are highly dynamic environments where keratinocyte proliferation, fibroblast activity, angiogenesis and immune modulation must be carefully coordinated.

Cellular Senescence and Keratinocyte Proliferation

A review on the role of NAD^+ in regenerative medicine highlights that low NAD^+ promotes skin-cell senescence, while restoration of NAD^+ reduces senescence markers and improves keratinocyte proliferation and wound regeneration (21).

Kang et al. reviewed NAD^+-boosting strategies in skin anti-ageing and concluded that NAD^+ homeostasis is critical for both cell proliferation and wound healing; NAD^+ elevation promotes epidermal barrier repair, dermal matrix production and global skin rejuvenation.

Preclinical Wound Healing Models

Diabetic wound healing with NMN: An NMN-loaded thermosensitive hydrogel enhanced wound closure, angiogenesis and collagen deposition in diabetic rats, suggesting that local NAD^+ restoration can rescue impaired healing (22).

NR and resveratrol in diabetic wounds: Combined NR and resveratrol improved wound healing in diabetic rats via modulation of the unfolded protein response and NAD^+-linked stress pathways (23).

Nicotinamide in skin flaps: Earlier animal work showed that nicotinamide is angiogenic and accelerates wound healing and skin flap survival (24).

Clinical and Translational Implications

These data point towards NAD^+ restoration as an important regenerative axis in cutaneous surgery, plastic surgery, and chronic wound care—particularly in diabetic and elderly patients, who are over- represented in surgical populations.

VI. NAD⁺ Metabolism, Hair Follicles And Hair Growth

Mitochondria and Hair Follicle Cycling

Hair follicles have high metabolic demands, especially in anagen. A recent review summarizes growing evidence that mitochondrial dysfunction contributes to hair follicle degeneration and androgenetic alopecia, positioning mitochondrial health—and by extension NAD^+ metabolism—at the centre of hair biology (25).

NAD^+ Precursors and Hair in Preclinical Systems

NMN and hair growth: Xu et al. demonstrated that β-NMN promotes dermal papilla cell proliferation and hair growth in preclinical models, largely by reducing oxidative stress and supporting local NAD^+-dependent pathways (26).

Nicotinamide and hair-follicle biology: Nicotinamide (NAM) is a multifaceted skin molecule that restores cellular energy, improves DNA repair and reduces inflammation (27). However, some ex vivo data suggest that high-dose niacinamide can inhibit human hair growth and promote catagen in follicle organ culture models, (28) whereas other data indicate neutral or context-dependent effects. (29) This heterogeneity highlights the importance of dose, formulation and route (topical vs systemic).

Collagen + nicotinamide and hair growth: A recent rat study using recombinant humanized collagen combined with nicotinamide reported increased expression of basement membrane proteins and enhanced hair growth, indicating potential synergy between extracellular matrix support and NAD^+ precursors (30).

Human Data: NMN and Hair Quality

In 2025, Fukumoto et al. published a human trial in middle-aged women showing that oral NMN supplementation over 12 weeks improved hair quality and subjective perception of hair appearance, alongside other cosmetic benefits (31). While not a transplant population, this is the first controlled human evidence linking systemic NMN with improved hair parameters, and it aligns with preclinical findings that NAD^+ restoration supports follicular function.

Wound-Induced Hair Follicle Neogenesis

Wound-induced hair follicle neogenesis (WIHN) is a phenomenon wherein new hair follicles form de novo in the center of large full-thickness wounds in mammals, recapitulating aspects of embryonic hair development (32). WIHN is regulated by complex signalling networks (Wnt/β-catenin, IL- 6/STAT3, FGF, etc.) and involves both epidermal and mesenchymal compartments. While NAD^+ precursors have not yet been specifically studied in WIHN models, the established roles of NAD^+ in stem-cell function, inflammation and tissue regeneration suggest they may modulate these processes, with potential relevance to post-transplant peri-follicular remodeling and scar behaviour.

VII. Translational Implications For Surgery

General Surgery and Perioperative NAD^+ Repletion

From the above data, several themes emerge that are relevant to perioperative practice:

1. Organ protection: NR and NAM show cardioprotective and tissue-preserving effects in ischemia–reperfusion and sepsis models, suggesting a role in high-risk cardiac and major surgery (33).
2. Enhanced wound healing: NMN and NR improve wound closure, angiogenesis and dermal repair in diabetic and chronic wound models, supporting their use in plastic surgery, orthopaedics, vascular surgery and general surgery—especially in metabolically compromised patients (34).
3. Biological age modulation: NAD^+ precursors may help reduce biological age markers and improve resilience, potentially lowering perioperative risk in elderly patients (35).

Because rigorous, surgery-specific RCTs are still scarce, any integration of NAD^+ precursors into perioperative protocols should be regarded as off-label and hypothesis-driven, ideally within prospective registries or trials.

VIII. Specific Considerations In Hair Transplant Surgery

Hair transplant surgery imposes a unique set of demands: follicular units are dissected, stored ex vivo for variable intervals and re-implanted into a micro-wounded recipient bed, while donor areas must heal with minimal scarring and long-term stability.

On the basis of the data above, at least three conceptual roles for NAD^+ precursors can be proposed:

Pre-operative "Biological Prehabilitation"
Systemic NAD^+ repletion via oral NR or NMN for 2–4 weeks pre-operatively could:

Improve mitochondrial function and reduce oxidative stress in hair-follicle stem cells and dermal papilla cells (36);

Enhance endothelial function and microcirculation in scalp and donor tissue (37); Reduce baseline inflammatory tone and senescence in skin and adnexal structures (38);

This "biological prehabilitation" is conceptually similar to pre-habilitation programs in major surgery and may be particularly relevant in elderly, diabetic, smoking or high-stress patients undergoing large sessions.

Peri-operative and Early Post-operative Support

Although direct data in hair transplant patients are lacking, extrapolation from skin and wound models suggests that maintaining elevated NAD^+ peri-operatively may:

Improve keratinocyte proliferation and re-epithelialization at recipient and donor sites (39); Support collagen deposition and remodeling, potentially improving scar quality (40)
Enhance early anagen entry and shaft thickening by supporting follicular energy metabolism 41.

Potential additional, yet untested, avenues include adding NAD^+ precursors or their metabolites to graft-holding or irrigation solutions, though this currently rests purely on mechanistic reasoning from ischemia–reperfusion and dermal cell culture data.

Long-Term Regenerative Strategies

Given the links between mitochondrial dysfunction and androgenetic alopecia (42), long-term NAD^+ precursor supplementation could, in theory, complement established hair loss therapies by:

Supporting follicular stem-cell maintenance; Modulating micro-inflammation and oxidative stress; Enhancing the "background biology" in which transplanted and native hairs coexist.

The recent NMN hair quality trial provides early proof-of-concept in non-surgical individuals (43). Future studies in post-transplant patients are needed.

IX. Safety, Dosing And Regulatory Considerations

Human studies of NR and NMN at doses typically ranging from 250–2000 mg/day report good safety profiles, with mild gastrointestinal symptoms being the most common adverse events.(44) NAM has an extensive history of use as vitamin B3 and in dermatology (45).

Key points for clinicians:
Regulatory status: NAD^+ precursors are marketed as dietary supplements in many jurisdictions; they are not approved as drugs for surgical indications, and quality can vary among manufacturers.

Drug interactions: Although major interactions are not widely reported, careful consideration is needed in polypharmacy, oncology (where NAD^+ may influence tumour metabolism), and patients in clinical trials.

Special populations: More data are needed in pregnancy, severe hepatic/renal impairment and in combination with cytotoxic therapies.

Long-term use: While most data are reassuring, reports of context-dependent effects (e.g., altered ischemic tolerance in prolonged use in some models) (46) argue for individualized risk–benefit assessment.

In hair transplant practice, it is prudent to:
Use well-characterized, quality-controlled products; Document dosing, timing and outcomes; Explain to patients that use in this context is adjunctive and off-label.

Gaps in Evidence and Future Research Directions
Despite strong mechanistic appeal and encouraging preclinical and early clinical data, several gaps remain:

1. Randomized trials in surgical patients: Controlled trials of NR/NMN as part of perioperative optimization in cardiac, vascular, plastic and orthopaedic surgery are needed.
2. Hair transplant–specific studies: There are currently no dedicated RCTs evaluating NAD^+ precursors in hair transplant patients (pre-, peri- or post-operative). This is a clear opportunity for prospective registries and multicenter studies.
3. Optimal dosing and timing: The ideal dose, start time relative to surgery, and duration post- operatively are unknown and may differ between organs and patient populations.
4. Topical vs systemic effects: The contrasting data on topical niacinamide in hair follicles highlight that route

of administration matters; future work should compare systemic NAD^+ precursors, topical formulations and combination approaches (47).

5. Long-term outcomes: Effects on long-term graft survival, donor area stability, WIHN-like regenerative phenomena, and integration with other regenerative modalities (platelet concentrates, exosomes, microneedling, low-level laser) remain undetermined.

X. Conclusion

NAD^+ precursors such as NMN, NR and NAM occupy a promising intersection between metabolic medicine, regenerative biology and surgical practice. By restoring cellular NAD^+ levels, they can enhance mitochondrial function, reduce senescence and inflammation, and promote wound healing and organ resilience in multiple preclinical models, with early supportive evidence in humans (48).

In hair transplant surgery, NAD^+ precursors offer a rational strategy to improve the biological context for graft survival and regeneration—particularly in older, metabolically compromised or high-stress patients—though direct evidence is still limited. The recent emergence of clinical data linking systemic NMN to improved hair quality in non-surgical populations provides a crucial bridge between theory and practice (49).

Until well-designed trials are completed, the use of NAD^+ precursors in surgery should be framed as an adjunct rooted in strong mechanistic rationale and increasing, but still incomplete, empirical support. Surgeons and regenerative physicians are well-positioned to lead the next phase: designing ethical clinical protocols, monitoring outcomes rigorously, and helping to define when and how NAD^+ modulation can most safely and effectively be integrated into mainstream perioperative and hair transplant care.

Conflicts of Interest

The author declares no conflicts of interest related to this manuscript. Funding No specific funding was received for this work.

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