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Abeer Ali Ali Yossif
Department of Dermatology and Venereology, Faculty of Medicine, Tanta University, Tanta, Egypt

Al-Sayed Shaaban Hewedy
Department of Dermatology and Venereology, Faculty of Medicine, Tanta University, Tanta, Egypt

Nashwa Kamal Radwan
Egyptian Atomic Energy Authority, Egypt

Yasmina Ahmed El-Attar
Department of Dermatology and Venereology, Faculty of Medicine, Tanta University, Tanta, Egypt

Corresponding Author:
Abeer Ali Ali Yossif
Department of Dermatology and Venereology, Faculty of Medicine, Tanta University, Tanta, Egypt

The human amniotic membrane: From structure to dermatologic innovation

Abeer Ali Ali Yossif, Al-Sayed Shaaban Hewedy, Nashwa Kamal Radwan and Yasmina Ahmed El-Attar

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Abstract
The human amniotic membrane (HAM) has emerged as a novel biomaterial in dermatology, offering regenerative, anti-inflammatory, and antimicrobial properties that support its use in both therapeutic and aesthetic applications. This review provides a comprehensive overview of HAM's anatomical and structural composition, methods of processing, and its unique biological functions. A particular emphasis is placed on its dermatologic applications, including wound healing, psoriasis, skin rejuvenation, pigmentation disorders, Stevens-Johnson Syndrome, and hair regeneration. The article highlights HAM's potential to innovate clinical practice in dermatology and its growing relevance in tissue-based therapies.

Keywords: Amniotic membrane, dermatology, wound healing, regenerative medicine, tissue therapy

Introduction

1. Anatomy and Histology of the Amniotic Membrane

The fetal membranes are a complex structure essential for fetal development. They comprise two primary layers: the outer chorion, which interfaces with maternal tissue, and the inner amniotic membrane (AM), a thin (0.02-0.5 mm), translucent, avascular layer that encases the embryo and defines the amniotic cavity [1].

The AM develops from extra-embryonic tissue and includes both a fetal component (The chorionic plate) and a maternal component (the decidua). These layers are connected by chorionic villi, linking the cytotrophoblastic shell to the decidua basalis. Histologically, the AM comprises three layers: an epithelial layer, a thick basement membrane, and avascular mesenchymal stroma [2, 3] (Figure 1) [3].

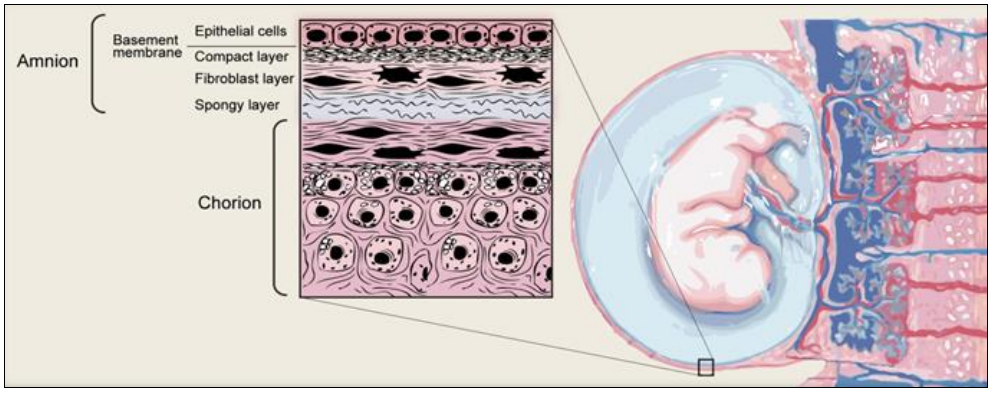

Fig 1: Anatomy and histology of the amniotic membrane [3].

Nourishment is supplied via diffusion from the amniotic fluid or the underlying decidua, as the AM lacks innervation and lymphatic or blood vessels [4]. The epithelial layer comprises a single row of cuboidal epithelial cells with microvilli, which support secretory and transport functions. Beneath it lies the thickest basement membrane among human tissues,

followed by the avascular mesenchymal stroma, which includes three sublayers: the compact, fibroblast, and intermediate (spongy) layers (1,5).

The compact layer forms the primary fibrous structure and contains collagens (types I and III), secreted by fibroblasts. Collagens V and VI provide filamentous connections with the basement membrane [5]. The intermediate (spongy) layer, adjacent to the chorion, features a non-fibrillar matrix rich in proteoglycans, glycoproteins, and mostly type III collagen. Its loose connection to the chorion allows the AM to be separated easily through blunt dissection [6] (Figure 2) [7].

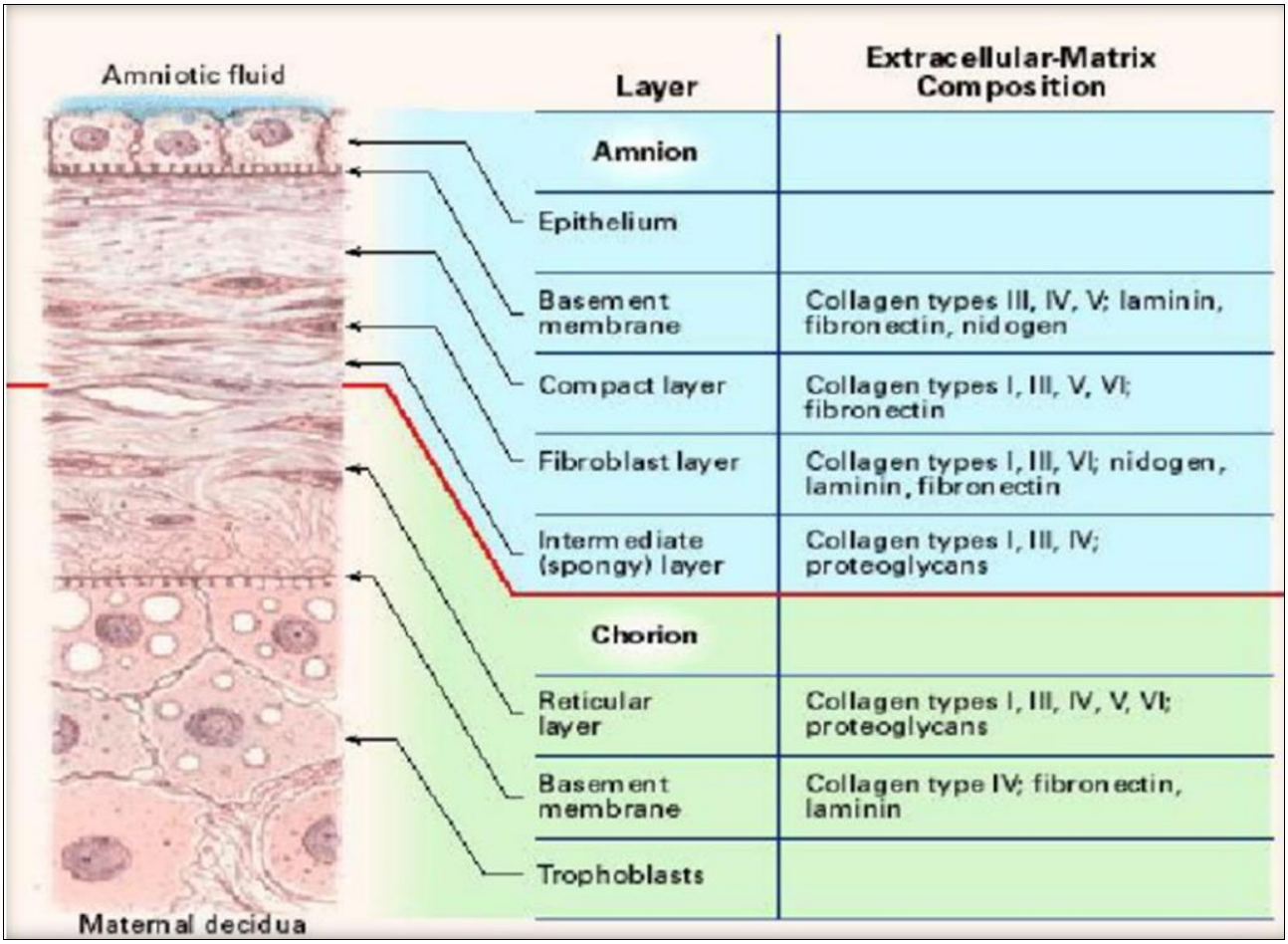

Fig 2: Schematic presentation of the structure of the fetal membrane at term. The extracellular matrix components of each layer are shown [7].

2. Processing of the Amniotic Membrane

Human amniotic membranes (HAM) are harvested from placentas obtained during elective cesarean sections, with prior written informed consent. Donor selection follows stringent criteria: absence of malignancy, infant malformations, or pathologies; gestational age ≥35 weeks; negative family history of genetic diseases; and no risk of infectious diseases such as HIV, hepatitis B/C, or syphilis [8].

After collection, the AM is washed thoroughly with sterile isotonic solutions (e.g., 0.9% sodium hypochlorite) to remove blood and debris. It is then air-dried and packed in polyamide bags. Sterilization is achieved via gamma irradiation using a 60Co source at 25 kGy, in accordance with International Atomic Energy Agency (IAEA) recommendations for tissue allografts [9].

3. Properties of Amniotic Membrane Derivatives

The HAM exhibits a range of beneficial biological properties, including:

Immunomodulation and Anti-inflammatory Effects: The AM does not elicit significant immune responses and suppresses proinflammatory cytokines such as IL-1α and IL-1β [10]. HLA class I antigens are expressed in amniotic epithelial and mesenchymal cells, while class II antigens are not, contributing to low immunogenicity [12].

Antiangiogenic and angiogenic Balance: The AM exhibits antiangiogenic properties through the production of endostatin, thrombospondin-1 (TSP-1), and tissue inhibitors of metalloproteinases (TIMPs). Conversely, it also contains angiogenic factors like VEGF and bFGF, indicating a complex regulatory role [11].

Antibacterial and Antiviral Effects: It produces antimicrobial peptides such as β-defensins and proteins like SLPI and elafin, contributing to its bacteriostatic and antiviral activity [14].

Promotion of Epithelialization and Scar Prevention: The AM facilitates tissue regeneration, enhances epithelial cell proliferation and migration, and minimizes fibrosis and scarring [13].

4. Clinical Applications of Amniotic Membrane

Thanks to its multifunctional biological effects - anti-

inflammatory, antimicrobial, antifibrotic, and antiangiogenic - HAM creates an ideal microenvironment for cellular adhesion and regeneration in both *in vitro* and *in vivo* contexts [15]. First used in skin transplantation by Davis in 1910 [16], its applications have expanded across various medical fields:

4.1 Ophthalmology
HAM is extensively employed in ocular surface reconstruction - notably for corneal and conjunctival repair. It functions as a biologic bandage, reduces inflammation, promotes epithelial healing, and is used as a patch or contact lens-like graft [17].

4.2 Orthopedics
Applications include tendon and ligament repair, management of cartilage degeneration, joint space restoration, and prevention of scarring and adhesions in spinal fusion surgeries [18].

4.3 Urology
HAM has been studied in urologic tissue regeneration, including bladder repair (first reported in 1982) [19] and treatment of urethral strictures, where it has demonstrated anti-fibrotic effects [20].

4.4 Dentistry and Periodontology
In dental and periodontal therapy, AM accelerates gingival regeneration, supports tissue adhesion, and facilitates antimicrobial protection. Promising results have been reported in cases such as buccal mucosal reconstruction post-leukoplakia excision [21, 22].

4.5 Oncology
Due to its pro-apoptotic, antiangiogenic, immunomodulatory, and cell-cycle regulatory properties, the amniotic membrane has emerged as a promising candidate in cancer research. Initial studies, beginning in 2008, demonstrated its anti-carcinogenic potential in various cancer cell lines [23].

4.6 Tissue Engineering
In regenerative medicine, the scaffold a supportive matrix for cell and tissue growth is critical. HAM is an excellent natural scaffold due to its biocompatibility, low immunogenicity, elasticity, mechanical strength, and permeability. Its ability to deliver growth factors and genetic material makes it suitable for diverse tissue engineering applications [24].

5. Dermatologic Applications of the Amniotic Membrane
5.1 Wound Healing
HAM was first used as a biological dressing for wound healing over a century ago. It minimizes infection, fluid loss, and pain while promoting rapid re-epithelialization in conditions such as burns, pressure sores, ulcers, and traumatic wounds [25, 26].

5.2 Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)
In these severe ocular complications, HAM serves as a biological dressing, reducing pain and inflammation while preventing scarring and promoting epithelium repair [27].

5.3 Skin Rejuvenation and Aging
The growth factors and cytokines in amniotic tissue - particularly EGF, TGF-β, and VEGF - support dermal fibroblast proliferation and collagen synthesis. This contributes to anti-aging effects and potential skin whitening through inhibition of melanogenesis [28].

5.4 Inflammatory Skin Disorders (e.g., Psoriasis)
HAM inhibits angiogenesis and fibrosis and promotes epithelial recovery. It has shown potential in psoriasis management, especially as an adjunct therapy using irradiated AM as a patch o.r graft [29].

5.5 Pityriasis Versicolor (PV)
Clinical trials have evaluated HAM combined with tea tree oil (TOSHAM) for treating PV lesions. The formulation leverages the antifungal and anti-inflammatory properties of both components, enhancing lesion resolution with fewer applications [30].

6. Hair Regeneration Potential
Amniotic fluid (AF) contains a rich mixture of bioactive components - including IGF-1, EGF, PDGF, IL-6, VEGF, and exosomes - that regulate hair follicle growth and transition to the anagen phase (15, 31, 32). AF-derived mesenchymal stem cells (AF-MSCs) stimulate follicular activity, dermal adipocyte expansion, and macrophage polarization, contributing to hair regrowth.

Conclusion
Human amniotic membrane and its derivatives have demonstrated impressive regenerative, immunomodulatory, and antimicrobial properties. Their clinical utility spans diverse medical fields, with expanding potential in dermatology, oncology, and hair regeneration. Ongoing research will continue to define its applications and mechanisms, making HAM an essential component in future biotherapeutic strategies.

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