GERIATRIC DERMATOLOGIC THERAPY

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ISBN
978-625-375-905-6

Publisher Certificate Number
47518

Book Title
Geriatric Dermatologic Therapy

Printing and Binding
Vadi Matbaacılık

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ORCID iD: 0000-0002-5807-6759

Bisac Code
MED017000

DOI
10.37609/akya.4051

Publishing Coordinator
Yasin DİLMEN

Page and Cover Design
Akademisyen Dizgi Ünitesi

Library ID Card
Geriatric Dermatologic Therapy / ed. Ümit Türsen.
Ankara : Akademisyen Yayınevi Kitabevi, 2026.
510 p. : figure, table. ; 195x275 mm.
Includes References.
ISBN 9786253759056

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PREFACE

As the global population ages, dermatologists face the unique challenge of providing effective care for the increasingly diverse and complex skin conditions that accompany aging. Geriatric dermatology has emerged as a vital subspecialty, bridging the gap between standard dermatological practice and the specific needs of older adults. This book is designed to serve as a comprehensive resource for healthcare professionals seeking to enhance their understanding of dermatological issues in the geriatric population. The skin, as the largest organ of the body, reflects not only the physical changes associated with aging but also the intricate interplay of genetics, environmental factors, and comorbidities that frequently accompany advanced age. Older adults often present with a variety of skin disorders, including but not limited to, xerosis, actinic keratosis, skin cancers, and the varied manifestations of chronic diseases. Their unique physiological changes require tailored approaches and considerations in diagnosis, management, and treatment. This book synthesizes current research and evidence-based practices in geriatric dermatology, emphasizing the importance of a holistic approach to patient care. It covers essential topics such as skin physiology in aging, common dermatological conditions, the impact of polypharmacy, and the psychosocial aspects of skin issues in older adults. By integrating clinical insights with practical guidance, this resource aims to empower healthcare professionals to deliver compassionate and competent care. We are grateful to the contributing authors, whose expertise and dedication have enriched this book. Their contributions reflect a wealth of knowledge and a commitment to improving the quality of life for our aging population. It is our hope that this work will inspire dermatologists, primary care providers, and other healthcare professionals to deepen their understanding of geriatric dermatology, ultimately enhancing the care and outcomes for older adults. In celebrating the uniqueness of geriatric dermatology, we welcome readers to explore the chapters ahead. Together, let us advance our knowledge and approach to the skin health of older adults.

Editor
Ümit Türsen

CONTENTS

Chapter 1 The Aging of the World's Population 1
Özge ZORLU

Chapter 2 Definition of Geriatry/Vulnerability/Frailty (Ageing, Frailty and Metabolic Changes)..... 5
Oğuzhan GÜMÜŞÇUBUK
Volkan ATMIŞ

Chapter 3 Dermatological Problems and Treatment in Long-Term/Nursing-Home Care 13
Özge ZORLU

Chapter 4 Skin Diseases of the Elderly 19
Özge ZORLU

Chapter 5 Geriatric Hair and Scalp Disorders 25
Sera Nur YÜCESOY
Zekayi KUTLUBAY

Chapter 6 Leg, Foot and Nail Diseases in The Elderly
(Leg, Foot and Nail Diseases in Elderly Individuals)..... 35
Ümit TÜRSEN
Nazlı CAF

Chapter 7 Superficial Mycoses in the Elderly 49
Mustafa ESEN
İsa AN

Chapter 8 Parasitic Skin Diseases (Parasitic Skin Infections)..... 61
Murat ÖZTÜRK
İsa AN

Chapter 9 Autoimmune Blistering Diseases in the Elderly..... 69
Abdullah DEMİRBAŞ
Semanur ÇAKIR SERİNBAŞ

Chapter 10 Adverse Drug Reactions on the Skin 81
Selen TANER AKBAY
Ümit TÜRSEN

Chapter 11 Leg Ulcers: Diagnostic Approach and Management 91
Düriye Deniz DEMİRSEREN
Rüveyda GÖNÜLAL BAK

Chapter 12 Atopic Dermatitis and Other Dermatitis (Atopic Dermatitis) 99
Elif COMERT OZER
Andaç SALMAN

Chapter 13 Lichen Planus 115
Erdinc TERZİ

Chapter 14 Lichen Sclerosus 133
Erdinc TERZİ

Chapter 15 Geriatric Psoriasis 147
Özge Sevil KARSTARLI BAKAY
Sevda EDİS

Chapter 16 Urticaria 153
Selcen HOŞGÖREN TEKİN
Andaç SALMAN

Chapter 17 Pruritus (Pruritus in the Elderly) 171
Özlem AKIN ÇAKICI
Andaç SALMAN

Chapter 18 Dermal and Skin Appendage Manifestations of Diabetes 181
Filiz CEBECİ KAHRAMAN
Sevil SAVAŞ ERDOĞAN

Chapter 19 Skin Manifestations of Diabetes in Geriatric Patients 191
Filiz CEBECİ KAHRAMAN,
Nurşad ÇİFCİ

Chapter 20 Non-Melanoma Skin Cancers (Management and Treatment in Geriatric Patients) 203
Berna SOLAK

Chapter 21 Melanoma (Management and Treatment in Geriatric Patients) 211
Berna SOLAK

Chapter 22 Cutaneous T-Cell Lymphomas (CTCL)
(Management and Treatment in Geriatric Patients) 217
Berna SOLAK

Chapter 23 Premalign and Benign Skin Tumors
(Management and Treatment in Geriatric Patients) 225
Berna SOLAK

Chapter 24 Paraneoplastic Dermatoses 233
Serkan YAZİCİ
Batuhan Mustafa DEMİR

Chapter 25 STIs (Sexually Transmitted İnfections) 241
Murat ÖZTÜRK
İsa AN

Chapter 26 Skin Infections 247
Erhan AYHAN
İsa AN

Chapter 27 Connective Tissue Diseases and Vasculitis
(Behçet's Disease and Other Vasculitis in the Elderly) 257
Defne OZKOCA
Seçil VURAL

Chapter 28 Cosmetic Procedures
(Cosmetic Applications in Geriatric Population) 267
Hanife UCGUN DEMİRTAS
Selami Aykut TEMİZ
Recep DURSUN

Chapter 29 Antihistamines 281
Özlem APTİ SENGKİOUN
Andaç SALMAN

Chapter 30 Topical and Systemic Steroids 287
Gizem DEMİR
Andaç SALMAN

Chapter 31 Topical and Systemic Retinoids in the Geriatric Population 295
Merve AKBAY
Sevilay ERTÜRK

Chapter 32 Topical and Systemic Antibiotics 307
Özlem DEVRAN GEVHER
İsa AN

Chapter 33 Topical and Systemic Antivirals 317
Kadir KAYA
İsa AN

Chapter 34 Corns and Calluses in the Geriatric Population 323
Aydan YAZICI

Chapter 35 Topical and Systemic Antimicotics 329
Mustafa ESEN
İsa AN

Chapter 36 Ciclosporin (Cyclosporine) 343
Suat SEZER

Chapter 37 Methotrexate 351
Özge Sevil KARSTARLI BAKAY

Chapter 38 Biologics (Use of Biological Agents in the Geriatric Patient Population) 357
Özge Sevil KARSTARLI BAKAY
Bengisu MERAL KETENCİ

Chapter 39 Small Molecules 369
Meryem AKTAŞ
Andaç SALMAN

Chapter 40 Ultraviolet (UV), Photodynamic Therapy (PDT), and Energy-Based Devices (EBDs) in the Geriatric Population 377
Hanife Ucgun DEMİRTAS
Selami Aykut TEMİZ

Chapter 41 Cryotherapy and Electrocoterisation 389
Sibel YILDIZ
Selami Aykut TEMİZ

Chapter 42 Dermatosurgery 395
Sibel YILDIZ
Selami Aykut TEMİZ

Chapter 43 Vaccination and Skin Tests (Vaccination & Skin Tests in the Elderly Population) 403
Adil ÖZCANLI
Seçil VURAL

Chapter 44 Nutritional Skin Diseases 409
Elif IRMAK YAZICI
Serkan YAZICI

Chapter 45 Skin Problems in Alzheimer Disease, Dementia and Other Cerebrovascular Problems 421
Elif DEMİRCİ SAADET

Chapter 46 Drug Metabolism in Geriatric Group 427
Kansu BÜYÜKAFŞAR
Çelebi ÇELİK

Chapter 47 Geriatric Pharmacotherapy in Dermatology and Adverce Drug Interactions 437
Arzu FERHATOSMANOĞLU
Serkan YAZİCİ

Chapter 48 Geriatric Dermatopathology and Immunopathology 443
Ayşe TÜRKMEN DEDEOĞLU
Yasemin YUYUCU KARABULUT

Chapter 49 Geriatric Dermoscopy 475
Muhammed Ali MERGEN
Tubanur ÇETİNARSLAN

Chapter 50 Geriatric Psychodermatology Approaches 483
İlayda Esna GÜLSUNAY
Aslı AKSU

Chapter 51 Future of Geriatric Dermatologic Therapy 487
Serkan YAZİCİ
Kaan Mert ÖZEL

Chapter 52 Improving Treatment Adherence in Geriatric Dermatology: Challenges and Practical Strategies 493
Belma TÜRSEN

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CHAPTER 1

THE AGING OF THE WORLD'S POPULATION

Özge ZORLU [1]

THE AGING OF THE WORLD'S POPULATION

Aging is an inevitable process and is usually measured by chronological age. Interest in aging dates back to ancient times. Cicero, a Roman politician and orator, wrote "De Senectute" (On Old Age) in 44 B.C. to lighten the common burden of old age.[1] Cicero gives ideas on preserving health and vitality in old age.

Because of diversity in genetics, lifestyle, and overall health, aging is not the same across the population.[2] Biological aging results from the progressive accumulation of cellular and molecular damage, which eventually reduces both physical and cognitive capacities, elevates disease risk, and leads to mortality. These changes vary widely, making chronological age an imperfect marker of the aging process.[3] Nonetheless, populations typically classify people aged 65 years and older as elderly.

Increasing longevity, coupled with sustained declines in fertility, has shifted population structures toward older age groups around the world. No country had > 11% of its population aged ≥ 65 in 1950, whereas the highest was 18% in 2000. However, this increasing trend is expected to intensify over the coming decades.[4]

The United Nations' *World Social Report 2023* projects that the population aged ≥ 65 will increase from 761 million in 2021 to 1.6 billion by 2050, more than doubling within this period. Growth is even steeper among those aged 80 and over, rising from 155 million to 459 million. Population aging affects all countries. It is projected that the ≥ 65 age group, which was 1 in 10 people in 2021, will account for 1 in 6 people worldwide in 2050.[5,]

Although population aging has been an ongoing phenomenon for more developed countries for many years, the populations of many low- and middle-income countries currently face rapid aging. Therefore, the distribution of the World's oldest countries is changing. Among regions, Europe and Northern America together account for the largest proportion of elderly individuals. Moreover, among countries, Japan, Italy, and Finland have the oldest populations. On the other hand, UN statistics forecast that Northern Africa, Western Asia, and sub-Saharan Africa will show the highest rates of increase in the elderly population during the next three decades (Figure 1 and Table 1).[5]

According to OECD (the Organization for Economic Co-operation and Development) data, nearly 18% of the population is ≥ 65 years old across the 38 OECD countries.[6] The speed of population aging varies across OECD countries. Although Japan has had rapid aging over the past three decades, Korea is expected to undergo the most rapid population aging among OECD members in the coming years. Regarding OECD partner countries, Brazil and China are the countries that are projected to have fast aging in the following decades (Figure 2).[7]

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DOI: 10.37609/akya.4051.c4781

issues, urinary incontinence, depression, or skin conditions. As a result of the increasing geriatric population, dermatologists will encounter many more geriatric patients with complaints that increase with age or new entities in the coming years. Older people frequently have skin diseases like xerosis, pruritus, dermatitis, infections, skin ulcers, or neoplasms. However, because of age-related skin changes, sometimes clinical presentation may become misleading. In addition, the co-occurrence of several systemic disorders in this age group and polypharmacy are challenges in the treatment of skin diseases.

Due to increased longevity and increasing the share of the old age population, novel guidelines and recommendations for skin care, prevention, and treatment of skin diseases are needed in this age group.

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CHAPTER 2

DEFINITION OF GERIATRY/VULNERABILITY/FRAILTY (AGEING, FRAILTY AND METABOLIC CHANGES)

Oğuzhan GÜMÜŞÇUBUK [1]
Volkan ATMIŞ [2]

INTRODUCTION

What is Ageing?

Aging is a time-dependent process in which the accumulation of multiple biological, physiological and functional phenotypic changes that takes more than decades to generate. This process is influenced by several factors notably genetics, environmental exposures and lifestyle options. Ageing is a complex trait regulated by numerous biological processes including cellular senescence, DNA damage, telomere shortening, epigenetic alterations and mitochondrial dysfunction (López-Otín et al., 2013; Campisi et al., 2019).

One of the important mechanisms of aging is the iflation of DNA damage. Over time, cells experience damage to their DNA from various sources, such as oxidative stress, UV radiation, and also replication errors. Cell's ability of repair this damage declines with time passes which lead to the accumulation of mutations and genomic instability (López-Otín et al., 2013). Telomere shortening is another important mechanism of aging. Telomeres which are the protective caps at the ends of chromosomes, shorten with each cell division. When telomeres become critically short, cells enter a state of senescence or apoptosis, contributiwhich contribute tissue dysfunction and aging (Blackburn et al., 2006).

Epigenetic changes, like DNA methylation and histone modification, also play an important role in aging. These modifications can change gene expression patterns, leadinwhich lead to the dysregulation of critical cellular processes. For example, age-related changes in DNA methylation patterns have been linked to the development of age-related diseases such as cancer or cardiovascular disease (Jones et al., 2015).

Another major mechanism leading to ageing is mitochondrial dysfunction. The power plant of the cell is mitochondria and they produce energy as ATP. As organisms age, mitochondrial function decreases and the amount of energy produced falls while production of reactive oxygen species (ROS) increases. Finally, this mitochondrial dysfunction results in cellular damage and plays a key role in aging (Finkel et al. 2007)

Chronic low-grade inflammation is also typical of ageing. It is hypothesised that various factors, including an accumulation of senescent cells, a higher microbial load and modifications in immune function lead to these chronic inflammatory responses. Inflammatory status is related with several age-related

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DOI: 10.37609/akya.4051.c4782

associated with ageing may pave the way for researchers to develop targeted therapies to alleviate age-related deterioration. Furthermore, examining the impact of the microbiome on ageing is emerging as an important area of research with potential implications for healthspan and lifespan (Franceschi et al., 2018).

Technological Developments

Wearable technologies and digital health applications help to monitor the health of elderly individuals and to determine daily life data more objectively. Fitness trackers and mobile health applications support patients to monitor physical activity and achieve goals. Artificial intelligence and big data analytics offer new opportunities for ageing research and clinical applications, increasing personalised intervention strategies (Topol, 2019). Telemedicine and remote monitoring systems have become increasingly important in the health management of older people, especially in the context of the COVID-19 pandemic. These technologies enable continuous monitoring of vital signs, early detection of health problems and timely interventions, reducing hospital visits and improving overall health outcomes (Giansanti, 2020).

CONCLUSION GENERAL EVALUATION

Ageing, frailty and metabolic changes are crucial factors affecting the baseline health status of older people. Understanding and managing these processes correctly has vital effects on the quality of life of the elderly population. Biological and physiological changes that occur during ageing increase the risk of frailty in individuals and lead to loss of independence in older people. Metabolic dysfunction is characterised by insulin resistance, dyslipidaemia and chronic inflammation and worsens the health problems and basic health conditions faced by the elderly.

New Approaches in Research and Clinical Practice

New research on the aging process and innovative methods in clinical practice have the potential to protect and improve the health of older individuals. Advances in genetics, epigenetics, wearable technologies and digital health applications hold promise for understanding ageing, managing health problems in the elderly and improving the health and well-being of the elderly population. The development of research into mechanisms and targeted interventions to address the health challenges associated with ageing will continue.

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CHAPTER 3

DERMATOLOGICAL PROBLEMS AND TREATMENT IN LONG-TERM/NURSING-HOME CARE

Özge ZORLU [1]

DERMATOLOGICAL PROBLEMS AND TREATMENT IN LONG-TERM/NURSING-HOME CARE

The world population is gradually growing and aging. The proportion of older people is increasing. Owing to the declining birth rate and increasing life expectancy, there is a decline in familial support for older people and an increased need for long-term professional nursing care.

Population aging leads to an increase in aging-related skin conditions and diseases. Some anatomical and physiological age-related changes make skin dryer, less resistant to environmental factors, and less regenerative compared to younger skin.[1-4] In addition, chronic systemic diseases, polypharmacy, and diminished attention to personal hygiene and skincare practices in older people further heighten vulnerability to dermatological problems.

Older people are commonly affected by dermatological disorders, including xerosis, pruritus, eczematous disorders, scabies, stasis dermatitis, pressure ulcers, skin infections, skin signs of systemic diseases, adverse drug reactions, cutaneous neoplasms, and so on.[3-6] Adequate skin care measures help prevent or delay age-related skin conditions and minimize their severity.[7] Therefore, appropriate skin care is crucial in daily nursing practice. In other words, in a long-term care setting, the nursing staff and dermatological consultations have an important role in skin care, prevention, and treatment of skin conditions and diseases.

Data on the epidemiology of skin diseases in nursing homes and long-term care facilities are limited.[8] However, every old person has at least one skin problem, most commonly xerosis cutis. Immobility and cognitive impairment may also limit the access of this population to specialized dermatological care. Healthcare professionals and nurses often focus on pressure injuries (PIs) and incontinence-associated dermatitis, but may overlook other skin conditions. On the other hand, infectious diseases and epidemics, such as scabies, can also pose significant problems during long-term care in nursing homes.

Most skin conditions and diseases encountered by the elderly are emphasized in the following chapters of this book, therefore only PI will be elaborated in this chapter.

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DOI: 10.37609/akya.4051.c4783

c) Use topical non-toxic antiseptics short-term to reduce bacterial burden with maintenance debridement. Options: iodine compounds *(povidone-iodine, cadexomer iodine—avoid in case of renal failure, thyroid disorder, known iodine sensitivity)*, polyhexanide and betaine, silver (*e.g., silver sulfadiazine*), chlorhexidine, sodium hypochlorite (*Use for short term only if no other option is available at <0.025% concentrations*), and acetic acid *(acidosis risk in extended periods over larger surfaces*). Do not use hydrogen peroxide due to its high toxicity.
d) Use systemic antibiotics in case of a clinical evidence of systemic infection. Limit the use of topical antibiotics.
e) If the bone is exposed, osteomyelitis should be assessed.

4) Wound dressing: Skin condition should be evaluated after every dressing.
   a) Hydrocolloid: for non-infected, clean, stage 2 and 3 PIs.
   b) Transparent film: for autolytic debridement (not for immunocompromised); secondary dressing for PIs treated with alginates or other fillers.
   c) Hydrogel: for shallow, non-infected, granulating, dry, painful, and/or minimally exuding PIs.
   d) Alginate: for moderate-heavy exudate PIs; also for infected PIs with concurrent treatment of infection.
   e) Foam: for exuding stage 2 and shallow stage 3 PIs.
   f) Silver-impregnated dressing: for infected, heavily colonized, or high infection risk PIs. Discontinue once infection is controlled. (Do not use in case of silver sensitivity)
   g) Honey-impregnated dressings: for stage 2 and 3 PIs. (Do not use in case of known honey sensitivity)
   h) Cadexomer iodine: for moderate-high exudate PIs. (Do not use in case of renal failure, thyroid disorder, known iodine sensitivity, lithium use, pregnancy, or breastfeeding)
   i) Gauze: do not use for open PIs that have been cleansed and debrided.
   j) Silicone: to protect fragile or friable periwound tissue from injury
   k) Collagen matrix: for nonhealing stage 3-4 PIs
5) Platelet-derived growth factors: for stage 3-4 PIs that have delayed healing.
6) Biophysical agents
   a) Direct contact electrical stimulation: for recalcitrant stage 2 and stage 3-4 PIs
   b) Pulsed electromagnetic field: for recalcitrant stage 2 and stage 3-4 PIs
   c) Pulsed radio frequency energy: for recalcitrant stage 2 and stage 3-4 PIs
   d) Ultraviolet C light: adjunctive option if traditional therapies fail; may reduce bacterial burden in critically colonized, debrided, and cleansed stage 3–4 PIs
   e) Low frequency ultrasound (USG): for debridement of necrotic soft tissue (not eschar). High-frequency USG, an adjunct for the treatment of infected PIs
   f) Negative pressure wound therapy: early adjuvant for stage 3–4 PIs. Avoid in inadequately debrided, necrotic, or malignant wounds; in wounds with exposed vital organs or without exudate; or untreated coagulopathy, osteomyelitis, or local/systemic infection is present

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CHAPTER 4

SKIN DISEASES OF THE ELDERLY

Özge ZORLU [1]

SKIN DISEASES OF THE ELDERLY

Changes in the Aging Skin

Aging is a chain of events that occurs over time. The skin is the organ that most clearly reflects aging. Two types of skin aging have been defined: chronological (intrinsic) aging and photoaging (extrinsic). While chronological aging reflects physiological, natural, and metabolic changes in skin structure and function, photoaging is mostly caused by UV light and is more pronounced in sun-exposed skin. It is thought that genetic, inflammatory, and hormonal factors, and cellular aging, which occurs with telomere shortening, lead to intrinsic aging. On the other hand, in addition to UV light, factors such as ionizing radiation, smoking, chemicals, environmental pollution, and lifestyle are thought to play a role in extrinsic aging.[1,2] Changes in the aging skin are presented in Table 1. UV lights accelerate the appearance of intrinsic aging findings in the sun-exposed skin. Solar radiation plays a role in the emergence of many dermatological problems, such as sagging and coarsening of the skin, wrinkles, easy bruising, itching, and blemishes. Signs of both intrinsic and extrinsic aging are observed in the aging skin.[1]

Table 1. Physiological changes in the aging skin.[1-3]

Age-related skin changes	Clinical significance
Decreased DNA repair	Photocarcinogenesis, increased malignancy risk
Reduced cellular renewal	Delayed wound healing and reepithelialization, roughness, uneven pigmentation
Decreases skin thickness, thinning of epidermis, dermis ve dermoepidermal junction, flattening of dermal papillae	Increased tendency to mechanical trauma and blister formation, increased risk of shearing and pressure injury
Fragmentation of collagen and elastic fibers	Impaired skin elasticity, wrinkles, skin laxing, increased risk of pressure injury
Decrease in vascular plexus	Purpura, delayed wound healing, impaired tissue perfusion, impaired thermoregulation, increased risk of stasis dermatitis/pressure injury
Decrease in melanocytes	Graying hair, increased susceptibility to solar radiation
Decrease in vitamin D synthesis	Osteoporosis, carcinogenesis risk

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DOI: 10.37609/akya.4051.c4784

Table 3. Skin findings of systemic diseases in elderly.(devamı)	
Cardiovascular diseases	Pallor, subungual splinter hemorrhage, pitting edema of the leg, Janeway lesions, Osler nodule, xanthoma, xanthelasma, amyloidosis, clubbing, cyanosis
Chronic renal failure	Dyschromia, pallor, xerosis, pruritus, purpura, calcinosis cutis, calciphylaxis, half and half nails, Muehrcke's lines, acquired reactive perforating collagenosis, nephrogenic fibrosing dermopathy, pseudoporphyria, porphyria cutanea tarda
Pulmonary diseases	Clubbing, cyanosis, sarcoidosis, yellow nail syndrome

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CHAPTER 5

GERIATRIC HAIR AND SCALP DISORDERS

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GERIATRIC HAIR AND SCALP DISORDERS

With advancing age, various changes occur in the hair and scalp of geriatric patients due to the physiological aging process. Hair loss and graying are the most common complaints during this process. In addition to aging, hormonal changes associated with menopause in women contribute to these changes, which tend to occur earlier in women compared to men. Alongside the physiological changes brought about by the aging process, pathological complaints related to the hair and scalp may also occur. This section discusses hair and scalp diseases affecting the geriatric population.

HAIR DISORDERS

Hair Aging

There are many factors that influence chronological hair aging, including both internal and external factors. Internal factors include the patient's race, gender, chronic diseases, dietary habits, and stress levels, while external factors include UV exposure and heat-based or chemical hair treatments. Hair aging encompasses changes in both pigmentation and the hair's moisture level, diameter, and density. As age advances, increased UV exposure is absorbed by light-sensitive amino acids in the hair, leading to increased free radical production. UVB exposure results in protein loss in the hair, while UVA primarily accelerates the whitening process. [1] Additionally, in smokers, cumulative effects over time lead to follicular inflammation, fibrosis, and a relatively hypoestrogenic environment due to increased pro-inflammatory cytokines in dermal hair papillae and inhibition of aromatase enzyme.[2] Chemical styling agents applied to the hair also cause damage, leading to a decrease in hair density over time.

Graying of the hair is one of the earliest signs of hair aging. Genetic and epigenetic factors, as well as ethnic characteristics, play an important role in the onset age of graying. In comparison to Caucasians, graying occurs later in Asian and African populations.[3] Graying results from a decrease in follicular melanocyte population and subsequent decrease in melanin production. This process is accelerated by UV exposure, smoking, and chemical hair treatments.

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DOI: 10.37609/akya.4051.c4785

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CHAPTER 6

LEG, FOOT AND NAIL DISEASES IN THE ELDERLY (Leg, Foot and Nail Diseases in Elderly Individuals)

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LEG DISEASES

Leg lesions in the elderly patients may present as skin dermatoses, cutaneous reflections of systemic diseases, paraneoplastic conditions, inflammatory diseases and benign or malignant neoplasms as in all ages and genders. In elderly individuals, the diseases mentioned below may also affect the foot and/or nail (1-2).

Xerosis cutis, or dry skin, is one of the most common problems in older individuals and is most commonly seen on the legs of older patients. The decrease in the activity of sweat and sebaceous glands in the elderly is the most significant factor leading to skin dryness. In advanced ages, inadequate desquamation of the skin, thickening of the skin, dehydration and skin barrier disorders contribute to dryness. Severe forms of dry legs may resemble "cracked porcelain" in dermatological examination, and the cause of these cracks is water loss from the epidermis, as significant deterioration occurs in the skin's barrier functions as the skin ages (2).

In the examination of xerotic skin, the skin appears thickened and scaly. Xerosis tends to be more severe, especially in winter when humidity is low. Exposure to air-conditioned environments in summer will also exacerbate dryness. It should be kept in mind that xerosis cutis is a major cause of pruritus and the cracked skin facilitates the entry of microorganisms. The care of xerotic skin in the elderly should be performed the daily basis. It is recommended to moisturize the skin with natural emollients to avoid xerosis. Additionally, mild soaps and bath oils can be used during the shower to preserve the skin's natural oils. Individuals should be advised to avoid scrubbing with exfoliating gloves or sponges during showers and to keep bath duration short. Additional treatments and recommendations can be tailored to the patient based on the severity of dryness (1-10).

There are many dermatological and systemic causes of pruritus, and special algorithms should be applied in the approach to itch. In this section, pruritus in elderly patients will be briefly mentioned. Pruritus is an itching sensation that is usually caused by xerosis, and xerosis is very common in the elderly, as mentioned above. The sensation of pruritus leads the person to scratch their skin, which causes inflammation and subsequently excoriations. In addition, the habit of scratching causes the skin to thicken, increasing the itching sensation, thus leading a vicious cycle of itching. Pruritus observed in the senile period may also result from the continuation of pre-existing skin conditions, such as atopic dermatitis, during the aging process. Besides, many underlying metabolic, paraneoplastic and/or psychogenic disorders may also cause pruritus in elderly individuals. Considering

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pagetoid reticulosis. However, there are also types of MF that, while not officially classified as variants, are given different names due to their distinct clinical presentations. These include hypopigmented MF, hyperpigmented MF, bullous MF, pigmented purpuric dermatosis-like MF, ichthyosiform MF, psoriasiform MF, verrucous MF, granulomatous MF, pityriasis lichenoides-like MF, papular MF and invisible MF. The clinical presentation and localization of each of the types listed are different. However, it is typical to see it in areas that are not exposed to sunlight, especially in classic MF disease. Involvement in the legs (thighs) and buttocks, which are the subject of this section, is quite common and should not be overlooked during examination (27).

In classic Mycosis Fungoides, about 10% of patients may have specific involvement of the palms or soles. However, there is also a rare form of MF known as "palmaris et plantaris," where the disease is either limited to or initially appears on the palms and soles. This form is particularly important due to its relevance to "dermatological foot diseases in elderly individuals," a topic covered in this section. Palmoplantar MF can clinically be confused with contact dermatitis, other types of dermatitis, moccasin type tinea pedis, verrucae, and hyperkeratosis. In cases of treatment resistance or suspicion, a biopsy should be performed for proper evaluation (27,28).

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CHAPTER 7

SUPERFICIAL MYCOSES IN THE ELDERLY

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INTRODUCTION

As the world's population grows every year, the number of elderly people is also increasing due to improvements in nutrition, housing and health care. In the United States, about 22 per cent of the population is expected to be elderly by 2050. In this case, the prevalence of dermatoses in the elderly population will also increase.[1] As we age, the skin, like all organs, is subject to inevitable changes. DNA repair, wound healing, immune system and mechanical protection are reduced. In addition, as we age, our skin is cumulatively exposed to many external physical and chemical factors such as ultraviolet rays, irritants and allergens over a longer period of time. With age, the epidermis becomes thinner and more sensitive. This facilitates the entry of microorganisms.[2] Fungal infections are the second most common dermatosis in the elderly after benign and malignant tumors. With ageing, co-morbidities such as chronic diseases and malignancies and polypharmacy increase. In addition, increased musculoskeletal problems, impaired vision, forgetfulness and increased dependence on others reduce compliance with treatment. This makes it more difficult to control fungal infections in the elderly.[1,2] Furthermore, there is a lack of treatment guidelines in the current literature to guide dermatologists in the management of superficial fungal infections in the elderly. This review aims to summarize superficial cutaneous fungal infections in the elderly in the light of the current literature.

DERMATOPHYTOSES

Tinea Pedis

Tinea pedis is the most common dermatophytosis. It is more likely to develop in alkaline pH conditions, high temperatures and when the skin of the foot is damaged. In the elderly, inadequate personal self-care, bed dependency, peripheral vascular insufficiency, obesity, diabetes, malignancy and other conditions that suppress the immune system increase the risk of tinea pedis. Elderly patients' generally poor vision and barefoot contact with contaminated surfaces facilitate infection. In particular, conditions where elderly patients are together, such as in nursing homes, also increase the risk.[1–3] The most common form of tinea pedis is the interdigital type, the others being chronic hyperkeratotic (moccasin type), vesiculobullous (inflammatory) and acute ulcerative. Itching is the most common complaint and may be accompanied by pain and burning. The secondary addition of bacterial agents can cause bad odors. Cellulitis and lymphadenitis can also develop. It is a disease that affects about 15-25% of adults.[2,3] In the Achilles survey, Piérard et al reported *a 9% increase in the prevalence of tinea pedis with each additional year of age* in elderly patients

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examination and 10-20% KOH examination of skin scrapings. Non-contact polarized dermoscopy and ultraviolet-induced fluorescence dermoscopy are also helpful diagnostic methods. Microbiologic culture is not recommended for the diagnosis of PV.[46] For PV, topical treatments would be the first choice for elderly patients because they are inexpensive, effective and safe. Because PV lesions can affect large areas of the body, the use of topical treatments can be relatively difficult for older people with physical disabilities and poor eyesight. Therefore, sprays and shampoos may be preferred for convenience.[7,49] Ketoconazole 2% cream, a lanosterol 14-a demethylase enzyme inhibitor from the imidazole group, may be used 2 times daily for 15 days. Other topical azoles can be used once daily for 2 weeks. Topical terbinafine 1% can be used 2 times daily for 7 days-4 weeks, 1% butefine 2 times daily for 2 weeks and 1% naftifine solution 1 time daily for 6 days. Ciclopirox olamine is recommended twice a day for 2 weeks. Other topical treatment options include zinc pyrithione, 2.5% selenium sulfide, propylene glycol, salicylic acid-sulfur combination, topical tacrolimus and topical cycloserine. It is important that any topical treatment be applied to the scalp, which is the main source of the fungus. Systemic therapy is recommended for the treatment of PV only in severe, recurrent cases and for prophylaxis.[7,49] A meta-analysis by Gupta et al. including 57 studies evaluating systemic ketoconazole, fluconazole, itraconazole, and pramiconazole in the treatment of PV recommended 200 mg/day for 5 days for itraconazole, 7 days for severe cases, 300 mg/day for 2 weeks for fluconazole, and 200 mg/day for 2 days for pramiconazole. Systemic ketoconazole is not recommended for the treatment of PV. PV recurrence rates within 1 year have been reported to be 60-67.5%. For prophylaxis, 200 mg itraconazole twice daily once a month is recommended.[49]

Pityrosporum folliculitis

Malassezia folliculitis is characterized by pruritic, erythematous follicular papules and pustules that usually appear in the second or third decade of life on the chest, back, neck, proximal arms, and less frequently on the face.[2,50] It is often misdiagnosed as acne vulgaris or bacterial folliculitis in young patients. However, severe itching, absence of comedones, and lack of response to antibiotics are suggestive. Predisposing factors include broad-spectrum antibiotics, systemic corticosteroids, immunosuppressive drugs, malignancy, HIV, sweating, and living in regions with hot and tropical climates.[50] It is rarely reported in the elderly. The literature lacks prevalence studies of Malassezia folliculitis in geriatric patients. However, since approximately 40% of MF patients have PV or SD, it can be assumed that there may be more undetected MF patients in the geriatric group.[46] *M. globosa*, *M. stricta* and *M. sympodialis* are often associated species.[50] Due to its high sensitivity and specificity, the KOH smear is primarily used for diagnosis. In elderly patients, systemic itraconazole 100-200 mg/day for 1-4 weeks and fluconazole 100-200 mg/day for 1-4 weeks may be used with caution for possible drug interactions. A combination of systemic and topical antifungals or tretinoin/benzyl peroxide may also be considered in appropriate cases. Nightly application of 2.5% selenium sulfide or daily washing with ketoconazole shampoo may be recommended as adjunctive therapy. It is also recommended to use selenium sulfide, topical azoles, or ketoconazole shampoo as a prophylactic treatment. [2]

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CHAPTER 8

PARASITIC SKIN DISEASES (Parasitic Skin Infections)

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INTRODUCTION

Globally, the elderly population is increasing, leading to an increase in geriatric health problems such as parasite infection. Arthropods, helminths and protozoa are the three main categories that cause disease in humans. Parasites can damage the skin and cause systemic diseases. While systemic parasite infections can be serious and life-threatening, cutaneous parasite infections usually cause discomfort and severe morbidity and can also be contagious, so recognition and prompt treatment of these infections is very important. Some biological factors that may increase health problems in the elderly are: age-related change or loss of the immune system, dysfunction of some vital organs, comorbidities, malnutrition, impaired personal hygiene due to physical disabilities, overuse or uncontrolled drug use. (1,2,3)

While scabies and lice infections occur worldwide and usually in older people, parasitic infections such as cutaneous leishmaniasis may occur in different geographical areas. Some difficulties may be faced when dealing with parasitic skin infections in older people. Clinical manifestations in older people may be non-classical and can be very diverse. Some conditions may occur mostly without itching and skin manifestations. This may be due to hypersensitivity reactions resulting from a weakened immune system in older people. This chapter describes the diagnosis and treatment of common parasitic skin infections (1,2,4,5)

SCABIES

The S. scabiei mite causes scabies in both humans and animals. The female mite lays its first egg a few hours after burrowing into the corneal layer of the skin and spends the rest of its four to six week life at the end of the tunnel. Inside the tunnel, the female mite feeds, lays eggs and produces faecal pellets. The resulting larvae move to the surface of the skin where they move freely before burrowing back into the stratum corneum to feed. In about two weeks, the larvae develop into adult mites and the cycle begins again. (4)

EPIDEMIOLOGY AND CLINICAL FINDINGS

Age-related data show that scabies is more common in children, young adults and the elderly. Scabies is more common in autumn and winter. There is a negative association between air temperature and scabies incidence, and a positive association with humidity.

It is most common in low and middle income tropical countries. It can be transmitted by close and prolonged person-to-person contact or sexually and affects people of all races and social classes. It is most

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CHAPTER 9

AUTOIMMUNE BLISTERING DISEASES IN THE ELDERLY

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INTRODUCTION

Autoimmune blistering diseases (AIBDs) represent a group of rare yet significant dermatologic conditions characterized by the formation of blisters and erosions on the skin and mucous membranes. While these diseases can affect individuals of all ages, they often present unique challenges in older populations. The elderly population comprises individuals aged 65 and above(1). While developing nations like Turkey currently exhibit lower ratios of elderly citizens compared to European counterparts, a rapid escalation is anticipated, particularly in the ensuing decades. Based on OECD data, the proportion of the elderly population relative to the total population stood at 17.96% in 2022, with a global upward trend. Projections suggest the population aged 60 and above will swell to 2.1 billion by 2050(2). The aging process is accompanied by increased UV exposure, comorbidities, polypharmacy, and a reorganization process involving the immune system called immunosenescence, all of which increase susceptibility to AIBDs (3). The primary alterations observed in the immune system of the elderly include chronic basal inflammation, reduced Langerhans cell count, diminished regulatory CD4 + CD25 + T-cell population and CD4 / CD8 ratio, and the generation of lowaffinity, ineffective immunoglobulins (4). In addition to immune dysfunction, aging also leads to weakening of the extracellular matrix, biomechanical properties of cells, and dermoepidermal junctions, making them less robust and delaying re-epithelialization and wound healing compared to younger skin. Specifically, weakening of dermo-epidermal junctions and flattening of dermal papillae occurs, which may increase the risk of blister formation (5,6). Blistering lesions can arise in dermatopathology, triggered by allergic, hypersensitivity, infectious, mechanical, metabolic, or other inflammatory factors. Edema and blistering lesions often manifest in the distal extremities among the elderly due to congestive heart failure (7). Moreover, scabies has garnered attention in recent years due to its rising incidence and resistance to treatment. Bullous lesions may also manifest in cases of scabies (8). Autoimmune blistering diseases (AIBDs) represent a group of diseases initiated by pathogenic antibodies, resulting in the development of bullous lesions on the skin and mucosa. This group includes Bullous pemphigoid, Cicatricial pemphigoid, Bullous lupus, Epidermolysis bullosa acquisita, Pemphigus vulgaris, Paraneoplastic pemphigus, Pemphigus foliaceus, IgA pemphigus and Linear IgA bullous dermatosis.

This section will delve into the epidemiology, clinical manifestations, diagnostic complexities, and therapeutic approaches, as well as the unique attributes of autoimmune blistering diseases commonly observed in the elderly. Furthermore, we will review the diagnostic modalities available for AIBDs, emphasizing their utility and limitations in older patients. Given

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ing degrees of success, including anti-inflammatory agents, systemic corticosteroids, immunosuppressive agents like rituximab, IVIg, plasmapheresis, and extracorporeal photochemotherapy(6). Dapsone, often used in combination with other therapies, may offer benefits, particularly in patients with dermal infiltrates containing neutrophils. Colchicine has demonstrated some clinical improvement as monotherapy or in combination with other immunosuppressants. Combining dapsone and colchicine with systemic steroids has shown efficacy. Cyclosporine and MMF(administered at doses of 2 to 3 g/day) have displayed promising outcomes when combined with systemic corticosteroids to induce disease remission. Similarly, AZA, dosed at 2 to 3 mg/kg/day, can be combined with systemic corticosteroid therapy for moderate to severe EBA cases. Despite treatment efforts, relapses are common due to the lack of specific therapeutic agents and the refractory nature of the disease. A metaanalysis examining 1,159 EBA cases reported from 1971 to 2016 identified intravenous immunoglobulin (administered at 2 g/kg for 3 consecutive days) and rituximab as associated with clinical disease remission. Notably, intravenous immunoglobulin was linked to complete remission in mechanobullous EBA, while no single drug therapy achieved complete remission in inflammatory EBA cases(15,28).

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CHAPTER 10

ADVERSE DRUG REACTIONS ON THE SKIN

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INTRODUCTION

Adverse drug reactions (ADRs) are defined as undesirable and unexpected harmful effects that occur when a therapeutic agent is used at normal doses for diagnosis, prophylaxis, treatment, or to alter physiological functions (1). ADRs can occur with any dosage of a medication. In elderly patients with multiple comorbidities and polypharmacy, unexpected hospital admissions are often caused by these unwanted side effects (1,2,3). This situation contributes to increased morbidity and mortality among older adults (2). Physiological, pharmacokinetic, and pharmacodynamic changes observed in geriatric patients can affect the absorption, distribution, and excretion of drugs (4). Increased sensitivity to drug effects in older individuals arises from changes in pharmacokinetics (how the body absorbs, metabolizes, and excretes drugs) and pharmacodynamics (the effects of the drug on the body) (5). Physical function losses, such as decreased glomerular filtration rate and reduced liver function, can heighten the susceptibility of elderly patients to adverse drug reactions (5). The most frequently observed ADRs include dermatological, gastrointestinal, and neurological symptoms (6).

The World Health Organization (WHO) categorizes drug reactions into six main types based on their characteristics (1,7,8). The most commonly identified clinical type of ADRs is Type A effects, which are dose-dependent and predictable (1,7). Type A effects account for approximately 80% of all ADRs (1,7,8). In Turkey, there is a lack of comprehensive epidemiological studies on ADRs. In a study conducted in the United States of America, the incidence of hospital admissions due to ADRs among geriatric patients was found to be approximately 10.5% (9). A similar study in Italy reported a rate of 6% among 1,756 geriatric patients, while a multicenter study in India found that 6.7% of hospital admissions for patients aged 65 and older were due to ADRs (7,10,11).

To prevent ADRs and achieve successful therapeutic outcomes in the geriatric population, patients should be thoroughly evaluated, and drug selection must consider patient-specific and age-related factors.

CLASSIFICATION

Various methods are used to classify adverse drug reactions (ADRs) (1,12,13). One classification system is based on the severity of the adverse event:

- **Minor ADRs**: Reactions that do not require treatment, are generally not serious enough to necessitate hospitalization, or are short-lived or treated with an antidote.
- **Moderate ADRs**: Reactions that require a change in medication, involve specific treatment for the

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DOI: 10.37609/akya.4051.c4790

Pustular Reactions

Acute generalized exanthematous pustulosis (AGEP) is a rare but serious pustular eruption, predominantly drug-induced, usually observed in middle-aged individuals (34). It is characterized by widespread erythematous macules and patches with multiple sterile pustules. Accompanying systemic symptoms may include fever, leukocytosis, and mild eosinophilia (34). Pustular psoriasis, which develops more slowly and has a chronic course, is differentiated from AGEP (20). It typically starts on the face and flexural areas. Treatment generally involves the immediate discontinuation of the offending drug. Corticosteroids may be used in cases of widespread disease. Recovery usually occurs rapidly, but despite a good prognosis, the presence of multiple comorbidities in older adults increases the risk of mortality and complications (20, 34).

Purpuric Reactions

Anticoagulant-Related Skin Necrosis

In elderly individuals, purpuric lesions are frequently observed due to skin aging, anticoagulant, and antiplatelet use. Anticoagulant-related skin necrosis arises primarily from the use of warfarin and heparin. Warfarin causes microvascular thrombosis in cutaneous venules, leading to hemorrhagic infarctions (35). This condition typically appears at the initiation of treatment, especially with loading doses. Sensitive erythematous plaques can ulcerate or develop into necrotic hemorrhagic bullae. Treatment involves discontinuation of warfarin and administration of vitamin K (35). Heparin-induced skin necrosis also predominantly affects women, similar to warfarin (35). It typically develops at intravenous or subcutaneous injection sites (36). Patients diagnosed with this condition cannot use heparin for life (36). Both drug reactions tend to have a more severe prognosis in older adults.

Drug-Induced Vasculitis

Drug-induced vasculitis is mostly observed as small vessel vasculitis (20, 37). It is typically characterized by palpable purpura on the lower extremities and can involve internal organs such as the kidneys, liver, and intestines. In cases of drug-induced vasculitis, perinuclear ANCA (p-ANCA) positivity is often detected (37). Treatment consists of discontinuing the offending drug and symptomatic management of the lesions. Systemic corticosteroids and immunosuppression may be necessary in severe cases.

Other Rare Reactions

Drug-induced subacute cutaneous lupus erythematosus (SCLE) is a reaction that often presents with cutaneous symptoms and is more common in women, particularly affecting the elderly (38). It typically appears as annular or discoid papules in sun-exposed areas (20). Common medications associated with SCLE include hydrochlorothiazide, diltiazem, verapamil, terbinafine, ranitidine, leflunomide, and certain chemotherapeutic agents (20, 38). Terbinafine, tumor necrosis factor-alpha inhibitors, antiepileptic drugs, and proton pump inhibitors have also been linked to this condition (20). The primary treatment involves discontinuing the offending medication.

Conclusion

Cutaneous drug reactions in the elderly can range from mild to life-threatening events. Physiological changes that alter drug metabolism, geriatric syndromes, polypharmacy, and multimorbidity are factors that increase the incidence of drug reactions in this population. Early recognition, prompt treatment, and close monitoring of all drug reactions are essential. To prevent drug eruptions in older adults, reducing unnecessary prescriptions and polypharmacy should be a goal, along with educating all healthcare providers on this issue.

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CHAPTER 11

LEG ULCERS: DIAGNOSTIC APPROACH AND MANAGEMENT

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INTRODUCTION

An ulcer is a disruption in skin integrity that leads to the loss of anatomical structure and function. It can be the result of either internal or external pathological conditions. Unlike erosion, which is the loss of only the epidermal layer, an ulcer involves the loss of both the epidermal and dermal layers. Chronic leg ulcers, most often found below the knee, are open wounds that do not heal in six weeks. While these ulcers can have numerous causes, most leg ulcers have underlying conditions such as arterial disease, neuropathy, and venous insufficiency. (1)

Leg ulcers are a common and serious problem in elderly patients. The presence of ulcers significantly affects the patient's quality of life. Risk factors include peripheral artery disease, autoimmune diseases, increased age-related chronic venous insufficiency, decreased mobility, and diabetes mellitus (DM). Leg ulcers seen in geriatric patients may become non-healing, chronic and have a higher risk of complications. These complications include infection, cellulitis, ischemia, and gangrene, all of which can potentially result in amputation. (2)

EPIDEMIOLOGY

Approximately 2.5 million people in the United States have leg ulcers (3). The incidence and prevalence of these problems increase as the population ages. A study has shown that over 85% of those affected are over 64 years old (4). Venous disease accounts for around 72% of leg ulcers, with 22% having a mixed venous and arterial origin. Only 6% are caused by purely arterial disease (5).

AGE-RELATED FACTORS IN LEG ULCERS

Leg ulcers are a common and worrisome problem among the elderly. Elements like aging skin, decreased mobility, daily living activities, and the numerous comorbidities prevalent in the elderly significantly contribute to the formation of chronic ulcers. These ulcers frequently arise from underlying conditions such as peripheral artery disease, venous insufficiency, autoimmune disease, connective tissue disorders and diabetes, all of which are more common in elderly patients (6). Consequently, addressing non-healing leg ulcers in the elderly necessitates a holistic and multidisciplinary strategy. Early diagnosis is crucial, as delays in treatment can lead to disease progression (7).

TYPES OF LEG ULCER

The three most common types of leg ulcers are **venous, arterial, and neuropathic** (2).

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DOI: 10.37609/akya.4051.c4791

timicrobial barrier against MRSA, Candida albicans, and Pseudomonas aeruginosa.

Topical Corticosteroids: Stasis dermatitis is often managed with compression, moisturizers, and short-term use of moderate-potency corticosteroid creams, followed by maintenance therapy at frequent intervals.

Antibiotics: Most chronic leg ulcers are colonized or contaminated with various microorganisms, commonly including S. aureus, P. aeruginosa, and Enterobacter species. Uncomplicated ulcers without signs of cellulitis or systemic infection do not require antibiotics. However, systemic antibiotics should be added if there are signs such as erythema, swelling, increased warmth, tenderness, or fever.

Anabolic Steroids: Anabolic steroids possessing fibrinolytic properties may be advantageous for treating acute and chronic lipodermatosclerosis and managing leg ulcers resulting from cryofibrinogenemia. However, their impact on the healing rate of venous ulcers has not been established.

Physical Modalities: Hyperbaric oxygen therapy, hydrotherapy.

Surgical Interventions: Pinch grafts, split-thickness skin grafts, epidermal and dermal grafts, composite grafts, saphenous vein surgery (45).

Patients with recurrent , who fail to respond to treatment within 2 weeks, who have peripheral arterial disease (e.g. ankle-brachial pressure index (ABPI) <0.8 or >1.2), or who have contraindications to compression therapy should be referred to a cardiovascular surgeon (46).

Prevention of Recurrence

Within 12 months, venous leg ulcers recur in 26-69% of patients. Particularly in ulcers persisting for more than one year, the recurrence rate exceeds 70%. There is evidence that compression therapy reduces recurrence (41).

CONCLUSIONS

Leg ulcers are a common and significant problem in the geriatric population. They are often caused by underlying conditions such as diabetes, venous insufficiency, peripheral arterial disease, connective tissue diseases, and are more common in older adults. Geriatric patients are also at higher risk of developing complications such as infection, cellulitis, and amputation, which significantly impact their quality of life and ability to function.

Consequently, addressing non-healing leg ulcers in the elderly necessitates a holistic and multidisciplinary strategy. Early diagnosis is crucial, as delays in treatment can lead to disease progression.

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CHAPTER 12

ATOPIC DERMATITIS AND OTHER DERMATITIS (Atopic Dermatitis)

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INTRODUCTION

Atopic dermatitis (AD) is a relapsing and chronic skin disease that can manifest as skin dryness, pruritus, and various forms of eczematous dermatitis. Allergic inflammation and skin barrier disruption play an important role in the pathogenesis of AD.[1] Currently, approximately 230 million individuals across the world are diagnosed with AD, making it the most common inflammatory skin disease globally.[2] The prevalence of AD in adults ranges from 1 to 3%, and it can either begin in adulthood or occur in forms persisting from the infantile or childhood period or recurring after several years.[3] With an aging population and social development, AD observed in the elderly has recently been recognized as a distinct clinical subtype. As a result, AD is now categorized into four separate phases: infantile (under two years old), childhood (two to 12 years old), adolescent/adult (12–60 years old), and elderly (over 60 years old).[4]

Elderly patients with AD have similar characteristic findings, such as male predominance, lower rates of lichenified eczema in the wrists and knee folds, and common patterns regarding the onset and clinical course of the disease.[5] In elderly patients, the course of AD requires different management approaches due to factors such as physiological aging, multimorbidity, polypharmacy, and functional dependency. Therefore, the diagnosis and treatment of this group of patients pose unique challenges.[6] In the management of these patients, it may be necessary to use strong anti-inflammatory drugs, such as systemic corticosteroids, in addition to standard treatments. Given that most elderly patients with AD struggle with this condition until the end of their lives, it can be considered a lifelong allergic disease.[5]

This chapter will focus on the epidemiology, physiopathology, clinical characteristics, and prognosis of AD in elderly patients.

EPIDEMIOLOGY

Over the past three decades, there has been a two-to-three-fold increase in the global prevalence of AD.[7] There are a relatively limited number of studies on the prevalence of AD in adult and elderly populations. Studies conducted in the previous decade found that the prevalence of AD in adults over the age of 20 years was 2%, while the one-year prevalence in adults over the age of 40 years was 0.2%.[8] In contrast, more recent studies indicate that the prevalence of AD in adults varies between 1 and 3%.[3] The lifetime prevalence of AD decreases with age. However, with growing industrialization, there has been a notable increase in the

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Accompanying pruritus is an important complaint in patients and can significantly affect quality of life. In cases of diagnostic uncertainty, a skin biopsy can be performed. Histopathological examination reveals acanthosis along with subacute eczematous findings. This may also be accompanied by superficial perivascular lymphocytic infiltration. Atopic dermatitis, contact dermatitis, nummular dermatitis, myxedema, cellulitis, and stasis dermatitis should be considered in the differential diagnosis of xerotic eczema.[127]

The most important step in treatment is skin hydration. Emollients with a high oil content should be applied twice a day. Application after bathing is particularly beneficial, as it enhances skin hydration. In mild cases, low- and medium-potency corticosteroids can be added to the treatment, while severe cases may require higher-potency corticosteroids for more rapid symptom relief, especially for pruritus.[128] However, it is essential not to neglect moisturization when using topical corticosteroids. Pimecrolimus 1% cream has also been found effective in controlling pruritus in xerotic eczema.[129]

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CHAPTER 13

LICHEN PLANUS

Erdinc TERZİ [1]

INTRODUCTION

Lichen planus (LP) is a chronic, immune-mediated, mucocutaneous inflammatory disorder[1]. The classic disease is defined by the so-called "rule six P", which summarizes the skin lesions' characteristics, i.e., planar, purple, polygonal, pruritic, papule and plaque[2]. Cutaneous LP is a rare dermatosis whose prevalence ranges from 0.22 to 1% and involves equally people of both sexes and different races. Instead, the more frequent oral disease occurs in 2 to 5% of the general population and is twice as common in women [3-6]. Although LP primarily includes the skin and oral mucosa, other mucous membranes and skin appendages, such as nails and hair, can also be damaged[5]. LP usually appears in middle-aged adults from 30 to 60 years of age and rarely affects other age groups[4].

Although the cutaneous disease has numerous clinical variants, its typical form is the classic LP, presenting with small, sharply demarcated, flattened and polygonally shaped erythematous-livid papules, which may coalesce as the disease progresses[4]. A prominent feature of LP is epidermal hypergranulosis, manifested as whitish reticulate structures or Wickham's striae on the lesions' surface[2]. A classic LP usually presents as localized form, with skin changes confined to the extremities, especially the wrists, ankles, dorsal surfaces of the hands and feet, and the lumbar region[2], or less commonly as a generalized condition, involving the entire body, including the oral and anogenital mucosa[4]. Despite the impressive clinical presentation, the latter has a good prognosis, marked by a spontaneous withdrawal within two years of onset [2]. Skin LP is generally followed by severe pruritus, whose intensity corresponds to the affected surface but lacks visible scratches or secondary infections[5].

Oral LP (OLP) occurs in about 70% of patients with classic skin disease, while in 20–30% of patients it represents the only manifestation of the illness. Although it can appear in six different forms, the reticular one predominates and is followed by the erosive form, characterized by pain, chronic, recalcitrant course, and possible malignant transformation into squamous cell carcinoma[6,7]. In addition, LP can affect the mucous membranes of the external genitalia, vagina, perianal area, urethra, conjunctiva, nose, larynx and oesophagus[5]. Lichen planopilaris (LPP) is a relatively uncommon form of the disease in which inflammation and keratotic papules surround the scalp hair follicles, eventually leading to scarring alopecia[8]. The follicular form of LP is fivefold commoner in women[4]. In 10% of patients with cutaneous LP, the disease affects few or all nails by the longitudinal ridging, splitting, thinning, and in uttermost cases, pterygium formation[9].

Recent studies have shown that patients with LP will more likely suffer from certain comorbidities[10,11]. The association of LP with a group of autoimmune diseases, namely liver disease, morphea, systemic lu-

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DOI: 10.37609/akya.4051.c4793

Consideration of drug-induced LP must always be explored prior to starting therapy. Withdrawal of the suspected drug leading to the gradual disappearance of lesions confirms the diagnosis, although it may take some time for lesions to fully resolve[160].

Prognosis

Cutaneous LP often clears spontaneously within 1 to 2 years, but residual hyperpigmentation is very common. Oral LP may clear spontaneously within 5 years, but typically it is a chronic disease with a remitting and relapsing course. Hair loss from LPP is permanent. Drug-induced LP lesions clear slowly after the causative medication is withdrawn.

Since the disease occurs at older ages, the side effect profile and comorbidities should be taken into consideration when choosing treatment, caution should be exercised due to the development of carcinogenesis, and patients with comorbidities should be followed more closely.

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CHAPTER 14

LICHEN SCLEROSUS

Erdinc TERZİ [1]

INTRODUCTION

Lichen sclerosus(LS) is a lymphocyte-derived skin disease that mostly affects the anogenital area, but can also affect any skin surface. Women are affected more than men[1]. The male-to-female ratio varies between 6:1-10:1[1]. It is more common in Caucasians. It can occur at any age. While it has the highest incidence in women in the two periods of pre-pubertal and post-menopausal, it is more common between the ages of 30-50. Reality Its prevalence is unknown. It is estimated to be between 1:300-1:1000. The majority of cases occur in post-menopausal women[2,3].

PATHOGENESIS

Genetic

Immune-mediated diseases have an immunogenetic scenario. A positive family history of LS in first-degree female relatives can be found in 12% of patients[4]. HLA-DR and DQ are supposed to be involved in the susceptibility and protection from LS[4]. In children with vulvar liken sklerosus (VLS), HLA-DQ7 was present in 66% of the cases, in comparison to 31% in controls. Although these children showed a low association with autoimmunity, up to 56% of their relatives presented another autoimmune disease [4]. In both adult male and female patients, HLA-DQ7 has been observed to occur more frequently in LS[4]. A study of UK women with VLS demonstrated an increased frequency of HLA-DR12 (DRB1*12) and a lower frequency of HLA-DR17 (DRB1*0301/04) compared to controls. Furthermore, HLA- DR and DQ could not be associated with the time of onset of VLS, anatomical changes and localization of the skin lesions, and the response to topical glucocorticoids[5]. In a cohort of Han Chinese women, the HLA- A*11, HLA-B*13, HLA-B*15, and HLA-DRB1*12 genotypes have been linked to a higher risk of VLS. Moreover, the women carrying HLA- A*11, HLA-B*15, HLA-B*35, and HLA-DRB1*12 genotypes were more susceptible to developing vulvar malignancy[6].

Epigenetic changes in LS may potentially induce malignant transformation. At the beginning of the disease, LS lacks p53 and CDKN2A mutations, suggesting that the cell-cycle regulation is not appreciably altered [4]. However, VLS is associated with altered isocitrate dehydrogenase, an enzyme responsible for DNA 5-hydroxymethylation patterns. As a consequence, the global methylation levels in the epidermis are diminished in VLS, and the UVA1 treatment could lead to a normalization of these levels [4].

It was described that a hypermethylation in p16INKa gene promoters could lead to an epigenetic silencing and, therefore, to an abnormal cell growth. This could be an early event in tandem with subsequent p53 somatic mutations, associated with tumor development and progression [4]. Furthermore, the p16INKa hypermethylation was linked to vulvar carcinoma arising from LS [4].

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Hydroxychloroquine	200mg/d PO 3months	Case report with resolution of the symptoms and modest clinical improvement	Nausea, diarrhea, skin rash, retinopathy, hemolytic anemia,
Antibiotics	Penicillin G benzathine 2.4Munits IM or Ceftriaxone 1 g IM every 2 weeks, next once a month	A 53,3% disease clearing with or without residual atrophy, after 3 to 9 months.	Injection site pain, type I hypersensitivity reactions, C. difficile-associated diarrhea
Sulphasalazine	1–2 g/d PO (long-term therapy)	Case report. Reduction of the skin infiltration after 1month	Headache, nausea, fever, skin rash, and reversible infertility in men, pancreatitis.
Vitamin D	Calcitriol 0.5µg/d PO 6months	Case report with clinical and histological improvement after 4–6months	Hypercalciuria
Baricitinib	2mg/d PO combined with PUVA twice-weekly	Case report in eLS with improvement of pigmentation and atrophy after three months	Not described in this case report.

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CHAPTER 15

GERIATRIC PSORIASIS

Özge Sevil KARSTARLI BAKAY [1]
Sevda EDİS [2]

INTRODUCTION

Psoriasis is an immune-mediated, chronic, inflammatory, systemic disease triggered by a combination of genetic and environmental factors. Typical lesions are characterised by squamous erythematous papules or plaques and may be localised or diffuse.[1] Psoriasis can occur at any age; however, there is a bimodal distribution in terms of age of onset; one is between 15-25 years and the other is between 50-60 years.[2]

Epidemiological studies reveal that psoriasis is the sixth most common skin disease in the elderly.[3] Psoriasis has been associated with several comorbidities, including inflammatory bowel diseases, hyperlipidaemia, hypertension, type 2 diabetes, obesity, cardiovascular events, and metabolic syndrome.[4]

Over the next few decades, the incidence of psoriasis is expected to increase with an aging and longer-living population.[5] Statistics show that the elderly aged 65 years and older will account for 20% of the US population by 2025.[6] There is limited data on the epidemiological, clinical, and genetic aspects of psoriasis in the elderly.[5] Furthermore, the management of psoriasis in the elderly can be challenging due to comorbidities and possible drug interactions.[7]

EPIDEMIOLOGY OF PSORIASIS IN GERIATRIC POPULATION

The exact prevalence and incidence of geriatric psoriasis is unknown. Considering the chronic course of the disease and the life expectancy of patients with psoriasis similar to the general population, the prevalence of psoriasis is expected to increase with age.[6]

In a population-based study of 132 newly diagnosed cases of psoriasis in the United States, the highest incidence rate was reported in the 60-69 age group.[8]. In the Far East, Yap et al. examined 2,571 patients aged 65 years and older who were outpatients at a tertiary referral centre in Singapore for 1 year and found the prevalence of psoriasis to be 3.1%.[9] In a larger and more recent study, Liao et al. found a similar prevalence rate of 3.9% in their cohort of 16,924 geriatric patients treated as outpatients over a 7-year period at a tertiary referral centre in Taiwan.[10] In Turkey, elderly patients with psoriasis accounted for 17.6% of the psoriatic population in the study by Sürgün et al.[5] Different studies have shown that the prevalence of geriatric psoriasis ranges from 5% to 34.5% of all psoriasis patients.[11,12] All these data point to the fact that geriatric psoriasis will continue to be one of the most important dermatological conditions

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capacity, medication history, carer status, financial needs, feasibility of follow-up and patient preferences.[6]

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CHAPTER 16

URTICARIA

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INTRODUCTION

The United Nations World Population Ageing Report and the World Health Organization (WHO) Scientific Group on the Epidemiology of Ageing define people aged 60 and over as elderly.(1, 2) Due to new medical treatment opportunities, technological advances and improving living conditions, the elderly population is increasing day by day in both developed and developing countries. WHO predicts that the population over the age of 60 will increase from 1 billion in 2019 to 1.4 billion and 2.1 billion in 2030 and 2050, respectively. (2) For these reasons, geriatric medical science is getting more and more attention every day. Urticaria is a common dermatological disease in all age groups, although it is most common in young adults.(3) In this section, the diagnosis, classification, differential diagnosis and treatment of urticaria will be discussed, focusing on the geriatric age group.

Definition and Classification

Urticaria presents with the development of wheals and/or angioedema. Wheals are characterized by sharply defined, superficial central edema, often with reflex erythema around it, that produces an itching or burning sensation and regresses in less than 24 hours. Angioedema is defined as deeper swelling that may last up to 72 hours, be erythematous or skin-colored, and accompanied by a burning, stinging, pain, or tightness sensation.(3)

Urticaria is classified as acute or chronic if symptoms last 6 weeks or less and more than 6 weeks, respectively. Chronic urticaria is classified as Chronic Spontaneous Urticaria (CSU) if the lesions occur spontaneously; and as Chronic Inducible Urticaria(CındU) if they occur with definite and reproducible triggers. Acute inducible urticaria is rarely seen. In CIndU, triggers can be a physical stimulus (physical urticaria) or urticariogen (contact urticaria or aquagenic urticaria).(3, 4) Unlike physical urticaria, non-physical urticaria types are not triggered by a physical factor. While active or passive heating triggers lesions in cholinergic urticaria, lesions occur in contact urticaria and aquagenic urticaria as a result of contact with the suspected agent and contact with water, respectively.(5) The classification of urticaria is summarized in Figure 1.

Types of CIndU can be listed as symptomatic dermographism, cold urticaria, delayed pressure urticaria, solar urticaria, heat urticaria, vibratory angioedema, cholinergic urticaria, aquagenic urticaria and contact urticaria.(3, 5) Apart from these, there are also delayed dermographism, cholinergic dermographism, cold-dependent dermographism, cold-triggered cholinergic reflex urticaria and rare types of

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DOI: 10.37609/akya.4051.c4796

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CHAPTER 17

PRURITUS (Pruritus in the Elderly)

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INTRODUCTION

Pruritus is the most common dermatologic symptom in the elderly.[1,2] Chronic pruritus, defined as itching lasting longer than 6 weeks, significantly impacts the quality of life in the affected individuals, leading to discomfort, sleep disturbances, and even psychological distress.[3-5] The etiology of pruritus in the geriatric population is not well understood; however, many older individuals experience pruritus not only due to dermatological conditions and xerosis but also as a result of various specific causes related to systemic disorders and medications.[6] Evaluating chronic pruritus in elderly patients can be difficult and in certain cases, laboratory tests and imaging methods may be required to make an accurate diagnosis. Understanding the underlying causes, mechanisms, and treatment options for pruritus in the elderly is crucial for effective management.

EPIDEMIOLOGY OF PRURITUS IN THE ELDERLY

As the global population ages, the prevalence of pruritus in older adults is becoming increasingly significant.[7] Using a standardized pruritus survey, the prevalence of itching was found to be 25% in Hispanic geriatric patients without dementia.[2] In a study evaluating 4,099 geriatric patients, the most common skin conditions in the elderly were eczematous dermatitis (20.4%), fungal infections (15.8%), and pruritus (11.5%), and the frequency of pruritus increased with age.[8] In another study, the prevalence of pruritus increased with age, reaching 45.9% in individuals aged 80 or older.[5] A large retrospective analysis of patients with chronic pruritus also revealed that patients over the age of 65 experienced significantly higher pruritus intensity compared to younger patients.[9]

CLASSIFICATION OF PRURITUS

There is limited data in the literature regarding the clinical classification of pruritus. It may be classified based on its duration as acute (lasting less than 6 weeks) and chronic (lasting more than 6 weeks).

The two-step itch classification developed by the International Forum for the Study of Itch offers a detailed approach to this subject.[3] The first step focuses on assessing the patient's clinical presentation and medical history, classifying them into three groups: Pruritus on diseased skin (Group 1), pruritus on non-diseased skin (Group 2), and chronic scratch lesions (Group 3). The second step involves an etiological classification based on the underlying causes, categorizing patients into six groups: dermatological, neurological, psychogenic/psychosomatic, systemic,

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DOI: 10.37609/akya.4051.c4797

Methotrexate	Inhibits dihydrofolate reductase	Psoriasis, dermatomyositis, bullous pemphigoid, pityriasis rubra pilaris, PN, AD
Phototherapy	Immunomodulatory, Reduction of pruritic cytokine release	Psoriasis, CTCL, AD, cholestatic itch, PN, HIV-associated itch
Dupilumab	Monoclonal antibody, blocking IL-4 receptor	AD, PN
Tralokinumab	Monoclonal antibody, blocking IL-13 mediated signaling	AD
Nemolizumab	Monoclonal antibody, IL-31 receptor alpha antagonist	AD, PN
Omalizumab	Monoclonal antibody, binds to free IgE	Chronic urticaria
Apremilast	Phosphodiesterase 4 inhibitor	Psoriasis; off-label use in AD, LP
Baricitinib, upadacitinib, abrocitinib	JAK inhibitors	AD

AD, Atopic dermatitis; PN, prurigo nodularis; CKD, chronic kidney disease related itch, CD, contact dermatitis; SNRI, selective norepinephrine reuptake inhibitor; LSC, lichen simplex chronicus; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant; H1 and H2, histamine receptors 1 and 2; GABA, gamma aminobutyric acid; NK1, neurokinin-1 receptor; LP, lichen planus; CTCL, Cutaneous T-cell lymphoma; IL; interleukin; JAK, Janus kinase; NP, neuropathic pruritus.

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CHAPTER 18

DERMAL AND SKIN APPENDAGE MANIFESTATIONS OF DIABETES

Hair and Nail Findings in the Geriatric Population with Diabetes

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INTRODUCTION

Diabetes mellitus (DM) is among the most prevalent endocrine disorders affecting the population. Elevated serum glucose levels result in damage to a wide variety of cell types, including endothelial cells, neurons, renal cells, keratinocytes, and fibroblasts.[1] The prevalence of DM is increasing globally, and the disease is becoming an epidemic and endemic problem with its significant economic burden.[2,3] The prevalence, comorbidities, and mortality rates of the disease are higher in the elderly compared to younger populations.[4] The aging of the skin and its appendages is a complex process involving genetic, endocrinological, immunological, and environmental factors, including free radical formation. With the growing elderly population and the increase in comorbidities such as DM, hair and nail disorders associated with aging are also becoming more common.

HAIR DISORDERS

At birth, the scalp contains approximately 1,000,000 hair follicles, with no new follicles forming after the fetal period.[5] It is estimated that a healthy adult's scalp contains between 80,000 and 120,000 hairs. As individuals age, there is a reduction in follicle density, decreasing from over 1,000 follicles/cm² in newborns to fewer than 500 in the elderly.[5] DM is characterized by hyperglycemia, which causes damage to various bodily systems, particularly blood vessels and nerves.[6] Hair follicles, similar to many other organs, are susceptible to hyperglycemic damage.[7] As blood circulates through hair follicles, proteins within the hair undergo glycation, and glycosylation increases in individuals with DM. Studies assessing the correlation between glucose variations in hair and glycated hemoglobin (HbA1c) have demonstrated a significant correlation between the glycation of the proximal 4 cm of hair and HbA1c levels. Hair samples of 12 cm in length roughly correspond to one year of tissue glycation and diabetic microvascular complications.[8-10]

It remains controversial whether DM-related hair disorders in the elderly are an aging process or a complication of the disease. However, it can be suggested that DM increases the frequency of certain hair disorders in the elderly.

Hair Graying

Hair graying is typically one of the earliest visible signs of aging, generally beginning in the 30s or 40s of age, although it can vary widely depending on genetic and lifestyle factors. Some research has suggest-

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inappropriate footwear, onychomycosis, and psoriasis, they can also be rarely linked to systemic diseases, such as DM, chronic renal failure, and systemic lupus erythematosus.[66, 74]

CONCLUSION

DM is one of the most prevalent endocrine disorders, and certain hair and nail findings are associated with it (Table 1). Hair loss and nail abnormalities are common complaints in elderly patients and may be related to or complicated by chronic diseases such as DM. While no hair or nail change is truly pathognomonic for DM, early diagnosis and proper management are crucial due to their significant impact on the patient's quality of life. Awareness of these conditions is essential for accurate diagnosis and optimal treatment. As the human population ages, the number of elderly individuals is increasing, and hair and nail disorders related to chronic diseases will become more prevalent.

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CHAPTER 19

SKIN MANIFESTATIONS OF DIABETES IN GERIATRIC PATIENTS

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INTRODUCTION

The definition of elderly is used for individuals over the age of 65. The science of geriatrics deals with topics such as internal diseases, social and functional lives, quality of life of these individuals. With aging, along with changes in organs and systems, the susceptibility to many diseases increases, and the course of these diseases may also be different from that of young people.

AGING

Aging is the irreversible loss of function that begins when we are born, progresses slowly over time, and occurs in all of our organs. The aging process is species specific and occurs under the influence of internal and external factors. Aging due to internal causes can be called spontaneous, natural, physiological or chronological aging. Chronological aging depends on unchangeable and unpreventable factors that occur in each individual and these are factors such as genetics, oxidative mitochondrial damage, telomere shortening or other mutations, hormones, inflammation and glycation. On the other hand, extrinsic aging depends on external factors such as sun exposure, diet, smoking, alcohol, drugs, and physical traumas. Amount of exposure to these factors and their effects vary for each individual. The influence of external factors can be reduced by self-protection. While aging slows down in the organs of a person who protects himself/herself from external factors, aging may accelerate in a person who does not protect himself/herself. In summary; internal aging is an unpreventable process, but external aging can be slowed down with the right lifestyle. It is also possible to delay internal aging by being well protected from external factors (1).

SKIN AGING

During the aging process, all organs lose their function simultaneously. Aging caused by progressive structural and molecular deteriorations also leads to loss of function and appearance changes in the skin. The causes of chronological aging and external aging in the skin are same with other organs. However, since the most common cause of extrinsic aging for the skin is the sun, it can also be called photoaging. Each of the cells in the skin has a different response to aging. The effects of chronological aging and photoaging on cells are also different (1-2).

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DOI: 10.37609/akya.4051.c4799

Skin Findings Due to Chronic Degenerative Complications of Diabetes	1. Diabetic dermopathy 2. Bullosis Diabeticorum 3. Diabetic Thick Skin • Diabetic hand syndrome • Scleledema diabeticorum • Dupuytren's contracture 4. Rubeosis Fasiei diabeticorum 5. Pigmented Purpuric Dermatosis 6. Diabetic Foot Ulcers 7. Erysipelas-like erythema/acral erythema 8. Acral dry gangrene 9. Calciphylaxis
Other Skin Diseases Common in Diabetes	1. Nekrobiyozis lipoidika diyabetikorum 2. Disseminated Granuloma annulare 3. Acanthosis nigricans 4. Acquired perforating dermatoses 5. Vitligo 6. Acrochordon 7. Generalized pruritus 8. Anogenital pruritus 9. Xerosis (dry skin) 10. Lichen planus 11. Hidradenitis suppurativa
Skin Diseases Develoing Secondary to Diabetes Treatment	1. Skin lesions due to insulin injection • Lipohypertrophy • Lipoatrophy • Local urticaria • Local calcification • Localized acanthosis (AN) nigricans • Insulin-related systemic allergic reactions 2. Reactions due to oral antidiabetics

pruritus and prurigo, xerosis, eczema and drug reactions. In addition, it should not be forgotten that there may be an increase in bacterial and fungal skin infections in the geriatric patient group due to decreased skin care, epidermal renewal and immunological functions. Skin findings of diabetes in elderly patients may be early indicators of systemic involvement (20).

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CHAPTER 20

NON-MELANOMA SKIN CANCERS (Management and Treatment in Geriatric Patients)

Berna SOLAK [1]

INTRODUCTION

Non-melanoma skin cancers (NMSC), particularly basal cell carcinoma (BCC) and squamous cell carcinoma (SCC), are the most common types of skin cancer worldwide. Unlike melanoma, the development of NMSC is more strongly associated with chronic sun exposure, which is the most significant modifiable risk factor. The incidence of these tumors has seen a marked increase with the aging global population, and they are more frequently observed in older adults. Factors contributing to their higher prevalence in the elderly include cumulative lifetime ultraviolet exposure, genetic predisposition, a decrease in the number of melanocytes with age, and the weakening of the immune system (immunosenescence) (1).

The management of non-melanoma skin cancers (NMSC) in the geriatric population requires a specialized approach due to age-specific challenges such as comorbidities, polypharmacy, and reduced skin healing capacity. Treatment strategies should aim to balance efficacy with the patient's overall health status, life expectancy, and quality of life. While surgical interventions are effective, they carry a higher risk of complications in elderly individuals, increasing the interest in minimally invasive treatment methods. This section discusses the approach and follow-up processes for managing non-melanoma skin cancers in the geriatric population.

ETIOLOGY AND RISK FACTORS

Immunosenescence refers to the structural and functional changes that occur in the immune system during the aging process and is believed to play a significant role in the development of NMSC in elderly individuals. During this process, the capacity of B lymphocytes to produce antibodies declines, the effectiveness of natural killer (NK) cells diminishes, and there are disruptions in the interactions between T cells and B cells. The reduced capabilities of NK cells contribute to the impaired recognition and elimination of tumor cells (2).

The most significant risk factors for non-melanoma skin cancers (NMSC) are age, genetic predisposition, and prolonged exposure to ultraviolet (UV) radiation from the sun. In elderly individuals, extended sun exposure, age-related changes in the immune system (immunosenescence), and other environmental factors emerge as key risk factors (2, 3). Basal cell carcinoma is typically associated with intermittent sun exposure, particularly during childhood, while SCC is linked to chronic UV exposure. Genetic mutations also play a significant role in the development of non-melanoma skin cancers (NMSC). In BCC pathogenesis, mutations such as the loss of the PTCH gene or uncontrolled expression of SMO lead to cell proliferation. SCC often arises from precancerous lesions like actinic keratosis, with errors in p53 signaling con-

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Follow-Up:

"In the elderly population, where non-melanoma skin cancers (NMSCs) can exhibit more aggressive behavior, the implementation of early diagnosis, treatment, and regular follow-up protocols is crucial for reducing disease morbidity. Post-treatment follow-up is particularly important for cancers such as high-risk squamous cell carcinoma. In these patients, who are at high risk for recurrence and metastasis, the follow-up process should be individualized, taking into account the patient's overall condition and comorbidities (1). Patients under long-term immunosuppression, such as organ transplant recipients, are at a higher risk of tumor recurrence, and the use of low-dose acitretin may be beneficial in these individuals. Additionally, immunosuppression should be maintained at the lowest effective dose possible (25).

Conclusion:

"In conclusion, a personalized treatment plan should be developed for each patient in the management of non-melanoma skin cancers (NMSCs), recognizing that surgical treatment may not always be the most suitable option. Healthcare providers should prioritize minimally invasive treatments, encourage shared decision-making with the patient, and oversee this patient population effectively through individualized management strategies.

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CHAPTER 21

MELANOMA
(Management and Treatment in Geriatric Patients)

Berna SOLAK [1]

INTRODUCTION

Melanoma has shown an increase in both incidence and mortality rates over the years, particularly in the elderly population (1). This increase is associated with longer life expectancy, increased UV radiation exposure, and age-related immunological changes (2). In the elderly, melanoma tends to be thicker, more invasive, and prone to rapid spread (3). Advanced melanoma has a high morbidity and mortality rate. Therefore, early detection and the tailoring of treatment strategies accordingly are crucial. In the geriatric population, the high prevalence of comorbidities, age-related immune system decline (immunosenescence), and expected life expectancy are critical factors that must be considered in treatment management (4). In this section, the approach to and management of melanoma in the geriatric population are discussed.

EPIDEMIOLOGY AND RISK FACTORS

The global incidence of melanoma is reported to be increasing by 2.6% annually, with this rise being particularly pronounced in the geriatric population. This increase is more marked in men, with age-standardized incidence rates reported as 3 per 100,000 for women and 3.8 per 100,000 for men (4, 5). Melanoma-related mortality also increases with age. Given that elderly patients are more likely to present with thicker and more aggressive tumors, age is recognized as a significant prognostic factor (3, 6). The primary risk factors for melanoma include a personal history of melanoma, exposure to ultraviolet radiation, fair skin, and a family history of melanoma (7).

In the geriatric population, cumulative and intermittent sun exposure over the years and age-related immune system decline are the primary factors that increase the risk of melanoma. The weakening of the immune system in older individuals (immunosenescence) leads to a reduction in natural immune responses against melanoma. The Wnt signaling pathway, which plays a role in cell growth and differentiation, is thought to be a significant mechanism affecting melanoma progression and treatment resistance through microenvironmental changes during the aging process (8).

CLINICAL FEATURES AND DIAGNOSIS

The diagnosis of melanoma is typically assessed during clinical examination using the ABCDE criteria (Asymmetry, Border irregularity, Color variation, Diameter >6 mm, Evolution). These criteria help identify the characteristic features of melanoma. Dermoscopic examination plays a crucial role in facilitating early diagnosis, particularly in the early stages. However, definitive diagnosis requires histopathological examination (5, 7).

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culty with self-examination and are at a higher risk of neglect. Follow-up care should be tailored according to the stage of the disease. In early-stage melanomas (Stage IIA and below), it is generally recommended to conduct follow-up visits every 6-12 months for the first 2-3 years. For advanced-stage melanomas (Stage IIB and above), follow-up, including imaging, is advised every 3-6 months for the first 2-5 years. After the fifth year, surveillance usually continues with annual visits (17). During follow-up visits, a full-body skin examination, lymph node assessment, and advanced imaging techniques should be performed as needed. Imaging modalities such as regional lymph node ultrasound, PET-CT, and brain MRI are recommended, particularly for patients with advanced-stage disease (4, 17). In the follow-up of patients, potential treatment-related side effects and other comorbidities should also be carefully considered (18). Therefore, follow-up should be personalized, taking into account clinical findings and the patient's overall health status. Additionally, patient education on topics such as self-examination and sun protection measures should be an integral part of the follow-up process.

Nutritional Status and Sarcopenia:

In elderly melanoma patients, nutritional status and sarcopenia can have a significant impact on treatment outcomes. Sarcopenia, defined as the age-related loss of muscle mass and function, is commonly observed in cancer patients as they age. Sarcopenia can increase the risk of complications during chemotherapy, immunotherapy, or surgical interventions, and may also weaken the response to treatment (19). Increased complications can make it challenging to continue treatment, thereby negatively affecting prognosis. Additionally, the impaired muscle function and low muscle mass associated with sarcopenia can further diminish overall quality of life. Therefore, the nutritional status of elderly melanoma patients should be carefully monitored, and appropriate nutritional support should be provided throughout the treatment process (11).

Palliative Care:

In advanced-stage geriatric melanoma patients, palliative care assumes an increasingly critical role. Palliative care focuses on pain management and symptom control, with the aim of improving the quality of life for both the patient and their family. In elderly patients, palliative care services should be initiated early and considered as an alternative to aggressive treatments (11). Psychosocial support is a crucial component of the treatment process for elderly melanoma patients. This support can reduce the risk of anxiety and depression, thereby improving treatment adherence and overall quality of life.

Conclusion:

In conclusion, the treatment and management of melanoma in elderly patients is a complex process that requires careful planning and monitoring tailored to the individual. Early diagnosis and treatment play a decisive role in prognosis, while age-related differences in treatment response, the presence of comorbidities, and the patient's overall condition must also be considered. Addressing these factors meticulously is essential for improving prognosis.

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CHAPTER 22

CUTANEOUS T-CELL LYMPHOMAS (CTCL) (Management and Treatment in Geriatric Patients)

Berna SOLAK [1]

INTRODUCTION

Cutaneous T-cell lymphoma (CTCL) encompasses a group of lymphoproliferative disorders characterized by the accumulation of T lymphocytes in the skin. The most common subtype of CTCL, mycosis fungoides (MF), typically begins as patches or plaques and may progress over time to tumors and extracutaneous involvement. The annual incidence of CTCL has shown a continuous increase since the 1970s; however, this rise appears to have plateaued in recent years (3).

EPIDEMIOLOGY AND RISK FACTORS:

Cutaneous T-cell lymphomas (CTCLs) are a rare type of lymphoma worldwide. In a study conducted between 1973 and 2009, the annual age-adjusted incidence of CTCL was reported to be 7.5 per million persons, with the incidence increasing with age and the highest rates observed in the 70-84 age group (3). In a more recent study, the incidence of CTCL in the United States was reported to have increased to 8.55 per million persons between 2000 and 2018, with this rise being particularly pronounced in older age groups (4). The increased incidence in the geriatric population is believed to be associated with factors such as the growing elderly population, increased immunosuppression, chronic inflammation, and chemical exposure in older individuals. Additionally, the incidence of CTCL is higher in males compared to females. Although this gender disparity has decreased over the years, the incidence rate remains higher in males (3-5).

Risk factors for cutaneous T-cell lymphomas include age, genetic predisposition, immune system disorders, certain viral infections, and prolonged exposure to UV radiation and environmental factors (e.g., chemical exposure). Additionally, the incidence of CTCL has been found to be associated with socioeconomic status, being more common among individuals with higher income levels (3, 4). This higher incidence is thought to be related to an increase in diagnoses due to easier access to healthcare services.

CLINICAL MANIFESTATIONS:

Cutaneous T-cell lymphomas present clinically across a broad spectrum and are rare globally. In the early stages, the disease typically manifests as itchy patches or plaques on the skin, which may thicken and evolve into tumors over time. In geriatric patients, age-related changes such as skin thinning and loss of elasticity can complicate the clinical course of CTCL, making diagnosis particularly challenging in the early stages. Mycosis fungoides (MF), the most common subtype of CTCL, generally follows a slow-progressing course (2, 6). However, in geriatric patients, due to the typically later-stage diagnosis of CTCL, there is a higher

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Primary Cutaneous Anaplastic Large Cell Lymphoma (PC-ALCL):

- **Surgical Excision and Radiotherapy (RT):** Main treatment methods for a single focus or localized disease.
- **Methotrexate (MTX):** Used in cases with multifocal lesions.
- **Brentuximab Vedotin (BV):** Shows promising results in refractory or recurrent cases.

Primary Cutaneous CD4+ Small/Medium T-Cell Lymphoproliferative Disorder (PCSM-TCLPD) and Primary Cutaneous Acral CD8+ T-Cell Lymphoma (ATCL):

- **Skin-Directed Therapies:** Excision, topical/intralesional corticosteroids, and radiotherapy are recommended treatments for localized disease.

Subcutaneous Panniculitis-Like T-Cell Lymphoma (SPTCL):

- **Oral Corticosteroids and/or Immunosuppressive Agents (e.g., Cyclosporine A, Low-Dose MTX):** Commonly used to achieve long-term remission.
- **Combination Chemotherapy:** Reserved for refractory cases or those complicated by hemophagocytic syndrome (HPS).

Primary Cutaneous Gamma-Delta T-Cell Lymphoma (PCGD-TCL) and Primary Cutaneous CD8+ Aggressive Epidermotropic Cytotoxic T-Cell Lymphoma (PC-AECTCL):

- **Multi-Agent Chemotherapy and Hematopoietic Stem Cell Transplantation:** Generally used treatment approaches for these aggressive subtypes.

Supportive Care and Quality of Life:

Cutaneous T-cell lymphomas (CTCLs) represent a challenging group of diseases due to their chronic course, the need for regular monitoring, ongoing tests, and continuous treatments, as well as the significant physical and psychological impacts, especially in advanced stages. For elderly patients, palliative care and the maintenance of quality of life are of critical importance in the management of CTCL. The incurable nature of these diseases often results in severe pain, skin deformities, and intense emotional stress, leading to a diminished quality of life. Elderly patients, in particular, may require multidisciplinary palliative care due to additional challenges. Palliative care aims to enhance quality of life by managing pain and other symptoms, providing nutritional support, and offering psychosocial support. Individualized care plans are essential to meet the needs of both patients and their families, supporting overall physical and emotional well-being (24).

Conclusion:

In the management of Cutaneous T-cell lymphoma (CTCL) in elderly patients, it is crucial to develop tailored treatment plans that address the specific needs of these individuals. Treatment options should be based on factors such as the subtype of the disease, its extent, and any systemic involvement, while also carefully considering the overall health status, existing comorbidities, and potential drug interactions in geriatric patients. Minimally invasive approaches, topical therapies, and low-dose radiotherapy should be prioritized in this patient group. Additionally, palliative care and symptom management should be at the forefront to enhance quality of life. Regular monitoring and effective management of side effects play a critical role throughout the treatment process. In conclusion, achieving optimal treatment outcomes in elderly patients requires multidisciplinary and individualized approaches.

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CHAPTER 23

PREMALIGN AND BENIGN SKIN TUMORS (Management and Treatment in Geriatric Patients)

Berna SOLAK [1]

INTRODUCTION

Premalignant skin tumors are lesions with the potential to transform into skin cancer. These lesions are quite common in the geriatric population and are frequently associated with factors such as prolonged sun exposure and age-related immune system weakening. Early diagnosis and appropriate management of these lesions are critical for reducing the risk of malignant transformation. The management of such lesions should be tailored to the specific needs of the geriatric population. Factors such as age-related physiological changes, comorbidities, immune system decline, life expectancy, and patient compliance should be considered in the management of these lesions in elderly patients. This section addresses how premalignant and benign skin tumors differ in the geriatric population and discusses the management of these lesions.

ACTINIC KERATOSIS (AK)

Introduction

Actinic keratosis (AK) is the most common premalignant lesion, confined to the epidermis, and composed of atypical keratinocytes that develop in areas of the skin exposed to UVB radiation. AKs possess the potential to progress to squamous cell carcinoma (SCC) over time. This condition is particularly prevalent in the elderly population. A meta-analysis has reported a global prevalence rate of 14% for AK, highlighting its significant worldwide disease burden. Furthermore, the study emphasizes that AK represents an increasing public health concern, with an incidence rate of 1928 per 100,000 person-years (1). Skin aging and immunosenescence in geriatric patients are among the factors that increase the risk of developing actinic keratosis (2).

Epidemiology and Risk Factors:

Actinic keratosis (AK) is more commonly observed in individuals with fair skin (Fitzpatrick skin types I-II), the elderly population, and males. Cumulative exposure to ultraviolet (UV) radiation throughout life is believed to play a fundamental role in the development of these lesions. Additionally, the risk of AK is reported to be higher in individuals with immunosuppression, such as those undergoing organ transplantation. (3-5).

Clinical Features:

Actinic keratoses typically appear on sun-exposed areas such as the face, ears, dorsal surfaces of the hands and arms, and the scalp. These lesions are characterized by their rough, scaly texture and reddish or brownish coloration. They are often small, numerous,

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DOI: 10.37609/akya.4051.c4803

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CHAPTER 24

PARANEOPLASTIC DERMATOSES

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ADVANCED AGE AND CANCER

In parallel with population growth, the population aged 65 and over is increasing rapidly all over the world. Aging is the most important risk factor for cancer development. The incidence of cancer increases with increasing age due to the cumulative effect of carcinogenetic factors, reaching a peak at 85-90 years of age.[1] Cancer-related deaths are second place after cardiovascular-related deaths in people aged 65 and over. 60% of newly diagnosed cancers and 70% of cancer-related deaths occur in the population aged 65 and over. In developed and developing countries, the cancers with the highest incidence in advanced age are prostate, lung and colorectal cancer in men, and breast, colorectal and lung cancer in women. In underdeveloped countries, the incidence rate of cervical cancer, hepatocellular cancer and oral cavity cancer, which are highly related to infection and socioeconomic conditions, is still high.[2,3]

PARANEOPLASIA

Paraneoplasia is defined as signs and symptoms that are independent of primary tumor invasion or metastases and are parallel to the presence of the tumor. It can occur at any stage of the disease in patients with malignancy and can lead to a wide variety of signs and symptoms. Paraneoplasia may occur during the course of a known tumor or may be the first and only symptom of an underlying occult tumor.[4,5] Awareness of common paraneoplastic conditions is of vital importance as it may allow an occult tumor to be diagnosed at an early stage. Sometimes it can be an indicator of a recurring tumor, as it can act as a tumor marker parallel to the tumor treatment response.

Although the first case of paraneoplasia was described in 1890 as peripheral nervous system involvement in patients with stomach, pancreas and uterine cancer, Guichard and Vigno used the term "*Paraneoplastic*" for the first time in 1949 when describing central and peripheral neuropathy in patients with metastatic cervical cancer.[6,7]

Until today, a spectrum of paraneoplasia affecting many organs or systems, especially in dermatology, has been described (**Figure 1**).[5,8,9]

PARANEOPLASTIC DERMATOSES

Paraneoplastic dermatoses are a heterogeneous group of dermatoses that occur due to internal malignancy and are not neoplastic in themselves. Many paraneoplastic dermatoses have been described in the current literature and new definitions are being made day by day. [5,8,10]

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CHAPTER 25

STIs (Sexually Transmitted İnfections)

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INTRODUCTION

Although levels of sexual activity generally decline with age after age 65, a large proportion of older adults seek sexual contact and engage in sexual activity. In one study, rates of sexual activity were higher among people in their 60s (71 % of men and 51 % of women were sexually active) and lower among people in their 70s (57 % of men and 30 % of women were sexually active) and 80s (25 % of men and 20 % of women were sexually active) than other older ages. (1,2)

Stigmatisation fear leads to less attention to safe sex behaviours in sexual activity in older age groups, which increases the spread of sexually transmitted infections in this age group. Persistent sexual activity is associated with the likelihood of the spread of sexually transmitted infections. In addition, older people have a weakened immune system, which makes them more susceptible to sexually transmitted diseases. The true incidence of sexually transmitted diseases may be higher than reported figures in the elderly population due to underreporting, missed diagnosis and non-inclusion of asymptomatic carriers. Sexually transmitted infections (STIs) among older adults have increased significantly, especially among divorced and widowed people.

Lack of knowledge about STIs among older people can lead to inaccuracies and untreated patients. There should be more programmes and research on the sexual health of older adults (1,2,3,4).

BACTERIAL DISEASES

Chlamydia

CT infection is usually a disease of adolescent girls and young women. It is most common in women aged 15 to 19 years and in young women because the target cell (a columnar epithelial cell, also known as a cervical ectopia, found in the ectocervix of young women) is replaced by squamous metaplasia with age. The reported incidence of CT infection among older adults (over 55 years of age) is 5 cases per 100,000 adults. However, these rates vary by racial and ethnic groups. (5)

CT can cause infections such as cervicitis, urethritis, proctitis, follicular conjunctivitis, epididymitis and pelvic inflammatory disease (PID). Most infections in young people are asymptomatic. There is no information on the number of asymptomatic infections in the elderly population. PCR analysis is the most sensitive tests for CT infection of the genital organs, including

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CHAPTER 26

SKIN INFECTIONS

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INTRODUCTION

Skin and soft tissue infections range from mild, self-limiting impetigo to life-threatening necrotizing fasciitis, encompassing a spectrum of diseases with various clinical presentations and etiologies (1). Bacterial skin infections are among the most common outpatient dermatologic diagnoses presenting to emergency departments and primary care providers. Skin and soft tissue infections are a growing threat to the health of an aging population (2).

AGE-RELATED CHANGES IN THE SKIN

Aging affects all components of the skin, including the epidermis, dermis, and subcutaneous layer. Proliferative activity of the skin decreases with age, leading to reduced epidermal renewal and thinning of the epidermis (3-6). This results in a less effective barrier, delayed wound healing, and increased opportunities for microorganisms to invade (4-6). Intradermal macrophages or Langerhans cells, responsible for cellular immunity, decrease by almost 50% as the skin ages (6,7). The resulting impaired cellular immunity increases the risk of infection and reduces the response to trauma and infection (4,8).

The dermis loses about 20% of its thickness over time, primarily due to the loss of collagen, elastic fibers, blood vessels, nerve cells, sweat glands, and sebaceous glands (5-8). Changes in collagen predispose aged skin to tearing and slow wound healing (4,5). The decrease in vascular structures leads to pallor, reduced inflammation, impaired delivery of cells to fight infection, and delayed clearance of foreign irritants (4,6). The gradual loss of nerve cells, sweat glands, and sebaceous glands results in dry and itchy skin with poor thermoregulation and decreased sensitivity to pain (6). The hypodermis also atrophies with age, making the body more susceptible to trauma and hypothermia.

RISK FACTORS FOR SKIN INFECTIONS

In addition to age-related changes in the skin, there are numerous risk factors that make the elderly susceptible to developing skin infections. Chronic diseases such as congestive heart failure, diabetes, and peripheral vascular disease impair vascular flow to the skin and extremities, and functional impairments such as immobility and incontinence in the elderly lead to skin breakdown and pressure ulcer formation, creating a substrate for infection (9,10). Nutritional deficiency is another significant risk factor for skin infections.

The presence of invasive devices such as indwelling urinary catheters, feeding tubes, and intravenous

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Table 1. Antibiotics for Skin and Soft Tissue Infections and Their Use in Elderly Patients (51) (Devamı)			
Antibiotics	**Scope**	**Route of administration**	**Considerations for Elderly Patients**
Vancomycin/Teicoplanin	Gram-positive bacteria, Staphylococci (including MRSA), Enterococci (excluding VRE)	I.V.	Risk of renal damage (vancomycin)
Daptomycin	Gram-positive bacteria	I.V.	Risk of rhabdomyolysis (evaluate drug-drug interactions)
Tigecycline	Active against many Gram-positive bacteria, Gram-negative bacteria (except Pseudomonas), and anaerobes	I.V.	Less well tolerated (nausea, vomiting)
Ceftaroline	Active against Gram-positive bacteria, Enterobacteriaceae (excluding ESBL), no activity against Pseudomonas	I.V.	
Dalbavancin	Active against Gram-positive bacteria, Staphylococci (including MRSA)	I.V.	Advantage: Long-acting, single administration
Oritavancin	Active against Gram-positive bacteria, Staphylococci (including MRSA), Enterococci (including VRE)	I.V.	Advantage: Long-acting, single administration

i.v., intravenous; MRSA, methicillin-resistant S. aureus; VRE, vancomycin-resistant Enterococci.

discharge and prompt treatment. A short course of antibiotic therapy may be beneficial due to its potential to reduce adverse events and antibiotic resistance, enhance patient compliance, and lower healthcare costs. Early discharge is particularly important for elderly patients to enable their return to routine activities.

Hospitalization in elderly patients can be associated with various complications. These conditions may include the exacerbation of pre-existing issues such as mobility and cognitive impairments, but also new complications that arise during hospitalization, such as delirium, hospital-acquired incontinence, falls, pressure injuries, and new functional impairments (52).

Long-acting antibiotics, including dalbavancin and oritavancin, may be beneficial in preventing hospitalization and associated complications in these patients. Furthermore, the single-dose administration of dalbavancin or oritavancin in patients with polypharmacy enhances compliance and reduces the risk of treatment failure. A recent study described the efficacy and safety of dalbavancin in elderly patients with various types of infections, including bone and joint infections, surgical site infections, and infective endocarditis. Clinical improvement was confirmed in 79% of elderly patients at 1, 3, and 6 months (53,54).

The therapeutic management of an elderly patient with a skin infection should be individualized based on the patient's profile. Patients with clinical stability, stable comorbid conditions, and stable social circumstances can be considered for early discharge and transition to oral therapy with an antimicrobial agent that has a good safety profile and simple route of administration. Conversely, in a patient with multiple comorbidities, polypharmacy, and the need for intravascular devices for drug administration, who can be defined as "sufficiently complex," the aim should be to simplify the treatment regimen (55).

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CHAPTER 27

CONNECTIVE TISSUE DISEASES AND VASCULITIS (Behçet's Disease and Other Vasculitis in the Elderly)

Defne OZKOCA [1]
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INTRODUCTION

The increase in the life expectancy and the quality of healthcare has led to an increase in the elderly population living with chronic diseases, including the connective tissue diseases and vasculitis. Alterations in the function of the immune system and other organ systems are seen because of aging, which not only changes the courses of chronic diseases but also the pharmacodynamics of the therapeutics.[1] This chapter will focus on the course and treatment of vasculitis, Behçet's Disease and connective tissue diseases in the elderly.

VASCULITIS IN THE ELDERLY POPULATION

Vasculitis is a term used to describe the histologic presence of inflammation on the blood vessel walls. The vasculitis are separated into primary and secondary vasculitis. Primary vasculitis are in turn grouped within themselves according to the size of the affected vessel. Secondary vasculitis occur due to an exposure or underlying disease. Medications, infections, malignancies and connective tissue diseases may lead to secondary vasculitis. An underlying malignancy or a newly started drug are common culprits of secondary vasculitis in the elderly. Large vessel vasculitis, medium vessel vasculitis and small vessel vasculitis are groups of primary vasculitis that may be seen in the geriatric population. Giant cell arteritis and polymyalgia rheumatica are the large vessels vasculitis that are observed in the elderly. Polyarteritis nodosa is the medium vessel vasculitis seen in the geriatric population; and the ANCA positive vasculitis are the small vessel vasculitis seen in the elderly. [2]

Giant cell arteritis, also known as temporal arteritis, affects the extracranial branches of the carotid artery. Its is more common in the females and elderly patients. The histopathologic specimen shows granuloma formation. The patients present with fever, constitutional symptoms, headache, claudication of the jaw and the tongue and scalp tenderness. The physical examination reveals absent pulses of the temporal arteries along with nodularity and tenderness on the tract of the temporal arteries. An elevated erythrocyte sedimentation rate (ESR) is observed in more than 80% of the patients. Vision loss due to the ischemia of the optic nerve is the most serious complication of giant cell arteritis. Glucocorticoid treatment should be initiated immediately to prevent vision loss. Aspirin is also helpful for the claudication. Acute mortality due to giant cell arteritis is uncommon however significant morbidity is observed due to optic nerve ischemia and glucocorticoid side effects.[2]

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DOI: 10.37609/akya.4051.c4807

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CHAPTER 28

COSMETIC PROCEDURES (Cosmetic Applications in Geriatric Population)

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ANATOMY OF THE AGING FACE

Knowledge of facial anatomy and the anatomical changes that occur with aging is essential for the accurate assessment and treatment of patients undergoing cosmetic procedures. Skin aging occurs due to two processes: chronological aging, which is an inevitable process related to the natural passage of time, and photoaging, which occurs as a result of chronic UV exposure. (1) Significant age-related changes in the appearance of the skin include dryness, wrinkles, laxity, and the development of benign and malignant neoplasms. The decline in skin functions associated with aging is numerous, including reduced sebum production, slowed chemical cleansing in the dermis, and delayed cell renewal. (2)

With aging, both the golden ratio (Phi) and neoclassical laws begin to change. The upper third of the face elongates due to the receding frontal hairline and brow ptosis, while the middle third remains relatively constant in proportion (although it may elongate with the drooping of the nasal tip). However, volume loss may occur in the midface due to fat redistribution and skeletal changes. The lower third of the face shortens due to perioral fat redistribution and significant resorption of the mandibular bone, which leads to the shifting of teeth and affects the aesthetic of the smile along with the lower face.

The appearance of an aging face is multifactorial and is not merely due to the downward sagging of the face caused by years of gravitational effects. Studies by Rohrich and Pessa have shown that there is no large, cohesive subcutaneous fat layer beneath the face; instead, there are multiple distinct compartments that operate independently. For example, the malar fat pad in the midface is composed of three separate compartments; as the size of these compartments changes, the ligaments separating them become more prominent, transforming a smooth, rounded, youthful appearance into a highly contoured aging face. Despite the perception that the face descends with age, it has been observed that the eyelid-cheek boundary does not change as one ages, and the location of moles in the midface region also remains unchanged with age. The "visible" wave of downward movement in aging faces is a result of changes in the subcutaneous tissues. (Figure 1)

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characteristics such as life expectancy, multimorbidity, polypharmacy, function, cognition, mobility, social support, and patient preferences when examining geriatric patients. (22).

In terms of aesthetic procedures, patients aged 65 and older differ from younger patient populations. More scientific research is needed to better address the needs of this growing patient group. Before any aesthetic procedure is performed, existing diseases and necessary treatments must be taken into account. For example, medications that interact with the coagulation system may be considered a relative contraindication for cosmetic injections.In this age group, dermal fillers, chemical and laser peels, and non-ablative photorejuvenation are effective methods, each of which can be used as standalone treatments. However, botulinum toxin (BTX) injections are often preferred more frequently in combination with other procedures. (23, 24)

Recommendations for elderly patients to protect their aging skin are as follows:

- Sun protection and avoidance of sun exposure in early life.
- Avoidance of oxidative stress factors (e.g., smoking, alcohol, lack of sleep, diet).
- Eating a healthy diet rich in fresh fruits and vegetables containing proven antioxidants such as vitamin C, resveratrol, lycopene, beta-carotene, vitamin E, flavonoids, and lutein. Avoiding high-glycemic index foods and grilled foods containing polycyclic aromatic hydrocarbons.
- Using pharmacosmetic products with evidence-based effects on the skin.
- It is recommended to prefer skin rejuvenation procedures such as fractional lasers, medium-depth chemical peels, photodynamic therapy, and cosmetics targeting collagen. (23)

When the literature is reviewed, there is limited information available on cosmetic applications specific to geriatric patients. The lack of knowledge and studies focused on the patient population aged 65 and older is noteworthy. However, as the elderly patient population increases, we believe that our knowledge, observations, and experiences in this area will inevitably grow.

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CHAPTER 29

ANTIHISTAMINES

Özlem APTİ SENGKİOUN [1]
Andaç SALMAN [2]

PATHOGENIC MECHANISMS OF ITCH

Itching, also known as pruritus, is characterized as an uncomfortable feeling that sets off the scratching response. Itching can evolve into chronic itch after an acute condition and can be classified as pruriceptive, neuropathic, neurogenic, and psychogenic itch. [1]

The pathogenic mechanisms of itch are quite diverse. Mediators that stimulate afferent nerve fibers and cause itch (biogenic amines, proteases, cytokines, and peptides) are known.[2] Although the most well-known pathway is histaminergic, itching is often initiated by a nonhistaminergic trigger, such as neurodegeneration and inflammation. [3]

Histamine

Histamine is the most widely recognized and researched pruritogen. The major source of histamine in the skin is the mast cell. Histamine degranulation from mast cells after allergen exposure reads, which interacts with sensory C fibers.[2] Histamine acts via G-protein coupled receptors, and four histamine receptors (H1R, H2R, H3R, and H4R) identified to date.[4]

Histamine, a biogenic monoamine and neurotransmitter, can have different effects depending on the receptor type.[5] The most common receptor of the subtypes is H1, which is primarily responsible for allergic symptoms and pruritus. Although H2 receptors are primarily responsible for gastric acid secretion, they have been shown to play a minor role in the etiology of itch in humans. [6,7] H3 receptors are found mainly in the central nervous system (CNS), while H4 receptors are found in hematopoietic tissues and neuronal cells. [5]

Antihistamines

Histamine receptor antagonists are effectively used in allergic and gastric diseases (anti-H1R and anti-H2R, respectively), while the effectiveness of other receptors is being studied in neurological and immune-mediated disorders (anti-H3R and anti-H4R, respectively).

H1 antihistamines suppress cutaneous vascular permeability, local vasodilation, and axon reflexes related to acute allergic reactions in the skin.[8] H1 antihistamines may also have anti-inflammatory effects due to their 'membrane stabilizing' properties on mast cells, basophils, and inflammatory cells.[9]

H1 receptor antagonists can be classified as first generation (hydroxyzine, chlorpheniramine, diphenhydramine, clemastine, etc.) and second generation (cetirizine, levocetirizine, loratadine, fexofenadine, bilastine, rupatadine, etc.). [5]

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DOI: 10.37609/akya.4051.c4809

therefore, dose adjustment is not recommended in patients with hepatic insufficiency. [11] Levocetirizine was found to have no effect on the QT interval.[39]

Rupatadine

Rupatadine undergoes presystemic elimination upon oral administration and is converted into various metabolites. Bile is the major route of excretion. Concomitant use of rupatadine and CYP-450 inhibitors is not recommended due to possible interactions. [40] Its use is not recommended since there are no studies on its safety in renal and hepatic failure. Rupatadine is recommended to be used with caution in patients with proarrhythmic conditions such as QT interval prolongation, hypokalemia, and bradycardia or acute myocardial ischemia.[11]

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CHAPTER 30

TOPICAL AND SYSTEMIC STEROIDS

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Andaç SALMAN [2]

PHYSIOLOGY OF AGING AND CORTICOSTEROID PHARMACOKINETICS

With advancing age, individuals show remarkable variability in their response to medications. This can partly be explained by age-related changes in major organ functions, the pharmacologic volume of distribution, and the composition of skin layers. Regarding primary sites where drugs are typically metabolized in the human body, due to lowered blood flow, liver and kidney function notably decrease with aging. (1,2) Therefore, these factors should also be kept in mind, when selecting any type of systemic therapy. When considering skin layers, the thickness of the epidermis decreases with age, along with flattening of the dermo-epidermal junction and atrophy in the dermis. Additionally, reduced hydration of stratum corneum may disrupt the absorption of hydrophilic topical drugs. Similarly, due to decreased lipid content in aging skin, impaired absorption of lipophilic topical medications would be expected. However, current studies have failed to demonstrate significant differences in the absorption of transdermal drugs according to the age of individuals.(3)

All corticosteroids are structurally based on four-ring cholesterol with three hexane rings and one pentane ring. Modifications to this core structure of steroid molecules result in different topical and systemic steroids with different potencies, glucocorticoid activity, and mineralocorticoid activity. Thus, some inactive steroids such as prednisone, must undergo hepatic conversion to become an active molecule -prednisolone-, which is particularly important for elderly patients with impaired hepatic functions. On the other hand, selecting a systemic glucocorticoid with minimal mineralocorticoid activity would

Table 1: Pharmacology of systemic glucocorticoids(GC)(5)

Glucocorticoid	Potency (Relative)	Mineralocorticoid Activity (Relative)	Duration of Action (Hours)
Cortisol (Hydrocortisone)	1	0.8	Short (8-12)
Prednisone	4	0.25	Intermediate (24-36)
Prednisolone	4	0.25	Intermediate (24-36)
Methylprednisolone	5	0	Intermediate (24-36)
Triamcinolone	5	0	Intermediate (24-36)
Dexamethasone	25-30	0	Long (36-54)
Betamethasone	30-35	0	Long (36-54)

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DOI: 10.37609/akya.4051.c4810

Immunosuppression-Infection	• Age • Underlying diseases • Concomitant use of immunosuppressive therapies or biologics(32)	• Decreasing dose and duration if possible	• Systemic examinations
Neurological/ Psychiatric effects	• Family history of depression/ alcoholism(33)	• Decreasing dose and duration if possible • Single morning dose • Addition of sedative drugs at night	• Assess symptoms including sleep disturbances, memory impairment, anxiety, agitation, hypomania, irritability, euphoria, depression etc.
Cataracts/Glaucoma	• Higher doses and longer duration (34) • Pre-existing ocular hypertension for glaucoma	• Referral to ophthalmologist patients with pre-existing risk factors	• Annual examination by ophthalmologist • Early referral when certain risk factors exist

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CHAPTER 31

TOPICAL AND SYSTEMIC RETINOIDS IN THE GERIATRIC POPULATION

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Sevilay ERTÜRK [2]

GENERAL CHARACTERISTICS AND MECHANISM OF ACTION

Retinoids are molecules derived from vitamin A and show structural and/or functional similarities to vitamin A. Retinoids have many significant functions, such as vision, bone growth and development, reproduction, cellular communication and differentiation, immune response, and tumor suppression [1].

Since they are not produced in the body, they need to be obtained externally through dietary intake. Vitamin A is consumed in two forms: vitamin A (retinol) and provitamin A (carotenoids). Both forms are stored in the liver. Keratinocytes in the skin convert and store most of the vitamin A as retinyl esters [2]. Retinoids are metabolized in the hepatic system and eliminated through bile or renal pathways [3].

Retinoids exist in natural and synthetic forms. The natural forms include retinoic acid, retinyl esters, retinol, and retinal . Retinol is the primary circulating form, while retinoic acid is the main active metabolite. Retinyl esters serve as the main storage and dietary form derived from animal sources. Additional dietary sources include provitamin A carotenoids such as beta-carotene, alpha-carotene, and beta-cryptoxanthin. Retinol circulates in the body bound to retinol-binding protein 4, the dominant form of vitamin A in circulation. The active forms of vitamin A include 11-cis retinal, 9-cis retinoic acid, and all-trans retinoic acid. 3,4-dehydroretinol (ddretinol), its ester (ddretinyl ester), aldehyde (ddretinal), and carboxylic acid (dd-retinoic acid) are unique retinoids also found in the skin [3]. Various synthetic retinoids have also been developed for the treatment of numerous dermatological conditions [4].

There are two main classes of receptors to which retinoids can bind: retinoid nuclear receptors and retinoid-binding proteins. Retinoid nuclear receptors are composed of retinoic acid receptors (RARs) and retinoid X receptors (RXRs). Each of these receptors has three subtypes: α, β, and γ, with different ligand-binding affinities . Retinoids exhibit most of their physiological effects by binding to RARs and RXRs in the nuclear receptor family, thereby influencing DNA transcription [5]. RARs bind to two main naturally occurring derivatives of vitamin A: all-trans and 9-cis retinoic acid, while RXRs bind only to 9-cis retinoic acid. Ligands that bind exclusively to RXRs are called rexinoids [3].

Retinoid-binding proteins are essential for the stabilization of hydrophobic retinoids in aqueous environments. Plasma retinol-binding protein (RBP 4), interstitial retinol-binding protein (RBP 3), and cellular retinol-binding proteins (CRBPs, including RBP 1, RBP 2, RBP 5, and RBP 7) are classified as such[3].

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DOI: 10.37609/akya.4051.c4811

that followed 299 patients for five years post-treatment found that 17% required two courses, 5% needed three courses, and 1% required 4-5 courses. Factors associated with the need for multiple isotretinoin treatments include a long history of acne, severe acne, low-dose treatment regimens, and women over 25 years old [40].

There are very few geriatric patients who continue to experience acne into their sixth and seventh decades of life. These patients have often undergone repeated acne treatments for 30-60 years. Studies to date have not identified geriatric-specific issues limiting the use of isotretinoin. However, serious adverse effects are more likely in older patients, which may require caution when prescribing isotretinoin. In a four-year follow-up by Seukeran and colleagues, 10 geriatric patients were treated with systemic isotretinoin. One patient received 1 mg/kg oral isotretinoin daily but could not tolerate cheilitis and developed hyperlipidemia. Subsequently, nine patients were treated with 0.25 mg/kg oral isotretinoin daily for six months. Acne was almost completely cleared in six patients within 3-4 months and in the other three patients within six months. Since geriatric patients responded well to low-dose isotretinoin with fewer side effects both in the short and long term, it was recommended that older patients be treated with a lower initial dose of 0.25 mg/kg/day and maintain the treatment for six months [41].

The side effects of systemic retinoids are detailed in Table 4. Contraindications for isotretinoin treatment include pregnancy, breastfeeding, uncontrolled severe hyperlipidemia, and hypersensitivity to retinoids or excipients [42].

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CHAPTER 32

TOPICAL AND SYSTEMIC ANTIBIOTICS

Özlem DEVRAN GEVHER [1]
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INTRODUCTION

Antibiotics have been used for many years and are one of the drug groups that have an essential place in treating skin diseases. After the discovery of penicillin, many antibiotics have been produced, both topical and systemic (1).

TOPICAL ANTIBIOTICS

Topical antibiotics are locally applied forms of antibacterial agents. With topical antibiotics, it is possible to reach high concentrations in the applied area with a smaller amount of drug. Advantages over systemic applications include ease of use, low potential for side effects, low risk of incompatibility, low cost and low risk of bacterial resistance (2). Many diseases coexist in the geriatric patient group, and multiple drug use is seen accordingly. Therefore, the use of topical drugs is safer in elderly patients (3).

Indications for use in skin diseases; *bacterial infections, wound and burn treatment, acne, rosacea, hidradenitis suppurativa, interventional treatments and eczemas, ulcers, and other secondary infected dermatological diseases* (4). Side effects such as allergic reactions and resistance development may be observed due to topical antibiotic use (5).

Physicians should use rational approaches to prevent antibiotic resistance. They should use drugs for the necessary indication, at the appropriate dose, for a sufficient period, and prevent unnecessary use.

Commonly used topical antibiotics in dermatology are as follows:

1. *Mupirocin*
2. *Fusidic acid*
3. *Clindamycin*
4. *Tetracycline and Oxytetracycline*
5. *Polymyxin*
6. *Neomycin and gentamicin*
7. *Bacitracin*
8. *Erythromycin*
9. *Metronidazole*
10. *Sodium sulfacetamide*
11. *Nadifloxacin*
12. *Nitrofurazone*

MUPIROCIN

Mupirocin is a fermentation product obtained from Pseudomonas flourecens and has a different structure from other systemic and topical antibiotics. It prevents protein and cell wall synthesis by reversibly inhibiting bacterial isoleucyl-tRNA synthetase. Mupirocin is bactericidal and is highly effective against aerobic

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The most common side effects are nausea, dyspepsia, anorexia, and, more rarely, gastrointestinal side effects such as vomiting, diarrhoea, constipation, pancreatitis, and hepatitis. Metronidazole causes a metallic taste in the mouth after systemic use. Serious side effects on the central nervous system are observed when used for long periods and in high doses. Ataxia, dysarthria, and cerebellar lesions have been reported after metronidazole use. Other side effects have been described as headache, dizziness, fainting, sleep disorders, confusion, excitation, depression, and peripheral neuropathy (50). Metronidazole increases serum levels of phenytoin, tacrolimus, cyclosporine, and warfarin. Dilsulfuram-like reactions may be observed with ethanol and protease inhibitors (34).

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CHAPTER 33

TOPICAL AND SYSTEMIC ANTIVIRALS

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TOPICAL ANTIVIRALS:

Due to the polypharmacy often seen in elderly patients and the potential side effects of systemic drugs, topical treatments are frequently preferred. Despite their widespread use, topical antivirals are less satisfactory than systemic antivirals in the treatment of herpes simplex infections (1). Topical antivirals are considered ineffective in Varicella Zoster Virus (VZV) infections and thus have no place in treatment (2).

TOPICAL ACYCLOVIR

Topical acyclovir has been shown to provide limited therapeutic benefit only in the early stages of recurrent herpes labialis when symptoms have begun but before the eruption has occurred. It is ineffective in the late phase of the infection (3).

TOPICAL PENCICLOVIR

Studies have shown that topical penciclovir is effective in the treatment of recurrent herpes labialis and is superior to 5% acyclovir cream. Unlike topical acyclovir, it stands out by demonstrating clinical efficacy even in the later stages of the disease. Penciclovir 1% cream is applied as early as possible to the herpes simplex lesions of the lips and face, every two hours during the day for four days. Erythema, edema, itching and dermatitis at the application site are among the rare side effects. Systemic absorption is negligible. It should not be applied to mucous membranes or the intraocular and periocular areas (3).

IMIQUIMOD

Imiquimod is an imidazoquinoline used as a topical immunomodulator. It enhances the immune response at the infection site, making it particularly important in the treatment of condyloma acuminata and molluscum lesions. Its role in herpes simplex infections is controversial. It is applied as a thin layer to the lesion area three times a week on non-consecutive days, left on for 6-10 hours, and then washed off. The treatment, which is generally applied for 8-10 weeks, has a maximum duration of 16 weeks. It is well tolerated, with minimal side effects. The most common side effect is localized erythema. Other side effects include itching, tenderness, burning/stinging, and pigmentation changes. No systemic side effects have been reported (3).

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DOI: 10.37609/akya.4051.c4813

Currently, two vaccines for zoster (Zostavax® and Shingrix®) are available. Both vaccines have been shown to be safe, elicit an immune response, and reduce the incidence of zoster and PHN. The recombinant zoster vaccine (Shingrix®) was approved in the United States in 2017 for the prevention of herpes zoster. The recombinant zoster vaccine (Shingrix®) appears to be superior to the live attenuated vaccine Zostavax® in terms of efficacy, cost, and its applicability to immunosuppressed patients (6,16,17).

SYSTEMIC ANTIVIRALS IN HSV INFECTIONS

In the elderly, HSV type 1 infection typically presents at the vermilion border of the lip. Oral mucosal involvement is rare. The primary concern with recurrent herpes labialis in the elderly is the potential for autoinoculation to the eyes or genital area. Acyclovir, valacyclovir, and famciclovir are the mainstays of treatment for HSV infections. There are recommended regimens for each of these for the treatment of primary and recurrent infections and for suppressive therapy (18).

A critical point in treatment is that the drugs must be initiated before the lesions become apparent. The presence of vesicles, except in chronic or widespread clinical presentations, indicates that treatment initiation has been delayed. Therefore, patients with recurrent HSV infections should begin their medication as soon as symptoms start.

Another issue in treatment is the occurrence of acyclovir resistance due to mutations in viral thymidine kinase, issues related to DNA polymerase, or other causes. In cases related to viral thymidine kinase, foscarnet can be effectively used. It is administered intravenously due to poor oral absorption. If the issue is a polymerase gene mutation, famciclovir may be effective (1).

SYSTEMIC ANTIVIRALS IN CUTANEOUS CMV INFECTIONS

CMV can cause cutaneous lesions, especially in HIV-positive individuals. CMV in the skin typically presents with ulcerative lesions in the genital area, perineum, and thighs. CMV has also been demonstrated in papular or purpuric widespread rashes, diffuse nodular and vesiculobullous rashes, and keratotic and necrotic skin lesions. Intravenous ganciclovir, foscarnet, and cidofovir, as well as intravitreal fomivirsen, are approved drugs for CMV infections (18).

SYSTEMIC ANTIVIRALS IN MOLLUSCUM CONTAGIOSUM

In immunosuppressed individuals, particularly those with AIDS, widespread molluscum lesions may be seen on the face. In such cases, classical topical and destructive treatments are generally insufficient, and antiviral and immunomodulatory drugs have shown promising results. There have been cases where successful responses were obtained with intravenous cidofovir (18).

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CHAPTER 34

CORNS AND CALLUSES IN THE GERIATRIC POPULATION

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INTRODUCTION

Numerous physiological and morphological changes occur in the human body with the aging process. The skin, as it interfaces with the external environment, is among the organs most affected by the aging process. In the elderly population, the feet deserve particular attention, not only because they bear the body's weight but also because they are prone to disorders such as diabetes mellitus (DM), peripheral arterial disease (PAD), and degenerative joint disease. Commonly seen hyperkeratotic lesions of the foot, such as corns and calluses, are dermatologic conditions that can significantly impair the quality of life in older adults.

Corns and calluses typically develop in areas exposed to repetitive mechanical pressure and friction, such as the plantar surface of the foot and the interdigital spaces. Age-related factors including thinning of the stratum corneum, decreased sebaceous gland secretion, reduced lipid and water content of the skin, diminished collagen quantity and quality, loss of subcutaneous fat and connective tissue, increasing prevalence of foot deformities, reduced muscle strength, and alterations in gait pattern contribute to the formation of these lesions. In addition to being a cosmetic problem, these lesions are clinically significant as they can cause pain, restricted mobility, postural instability, and an increased risk of falls, thereby contributing to higher mortality rates.

This section will discuss corns and calluses observed in the elderly population.

DEFINITION

Corns and calluses are forms of proliferative hyperkeratosis, commonly referred to as callus formation, that develop as a result of prolonged friction or mechanical pressure leading to thickening of the stratum corneum. This process initially represents a normal protective response of the body; however, when the thickening becomes excessive and symptomatic over time, it is regarded as a pathological condition.

EPIDEMIOLOGY

Except for the neonatal period, during which the skin has not yet been exposed to weight-bearing, callus formation may occur at any age in response to regular mechanical stress. Calluses are common dermatologic conditions that have maintained their clinical relevance from ancient times to the present day. Hippocrates emphasized the importance of physically removing hardened layers of the skin and developed

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DOI: 10.37609/akya.4051.c4814

When conservative treatments are insufficient, surgical intervention can be performed for the correction of existing anatomical deformities and the resection of prominent calluses. Surgical treatment can be effective in callus management when it targets the underlying mechanical cause and is performed in appropriately selected patients. In the geriatric population, surgical procedures should be undertaken with careful evaluation of surgical risks and comorbid conditions.[28, 29]

PROGNOSIS

If left untreated, corns and calluses may lead to painful gait, restricted mobility, bullous lesions, and infections. In geriatric patients, particularly those with underlying diabetes, such infections may result in amputation. Painful calluses in elderly individuals can also cause balance disturbances and falls, potentially resulting in life-threatening complications. Studies have demonstrated that the pain associated with calluses has a significant negative impact on patients' quality of life.[30]

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CHAPTER 35

TOPICAL AND SYSTEMIC ANTIMICOTICS

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INTRODUCTION

Currently, the lack of guidelines on the use of antifungal drugs in the elderly patient group brings difficulties in treatment management for dermatologists and all other physicians. Physiologic changes such as the decrease in glomerular filtration rate with age, the presence of concomitant diseases such as renal and hepatic insufficiency and polypharmacy increase the risk of drug-drug interactions. Additionally, factors such as forgetfulness, vision problems and muscle-joint limitations should be taken into consideration when choosing treatment for the elderly. Therefore, when managing the treatment of fungal infections, the pharmacokinetic and pharmacodynamic properties of antifungal drugs and potential drug interactions must be well known.

POLYENES

Polyenes were the first antifungals to be introduced into the market and brought to clinical use in the 1950s. Nystatin and amphotericin B are frequently used polyenes. They kill the fungal cell by irreversibly binding to ergosterol in the fungal cell membrane.[1]

NYSTATIN

Nystatin is one of three polyene derivatives in clinical use produced by fermentation by Streptomyces noursei. After irreversibly binding to ergosterol in the fungal cell membrane, it creates a pore on the membrane surface and kills the fungal cell by causing the leakage of essential intracellular components.[2] Nystatin was the first antifungal drug produced, but its use is limited to topical use because it is ineffective when taken orally and has severe toxic effects when taken intravenously. Nystatin is both fungicidal and fungistatic in vitro. Nystatin is ineffective against dermatophytosis caused by microsporums, trichophytons and epidermophytons. Nystatin is available in cream, ointment, powder, suspension, liquid and lozenge forms.[1,2] Although topical nystatin is still frequently used in mucocutaneous fungal infections caused by C. albicans, C. parapsilosis and other Candida species, its inadequate efficacy has been reported in many studies. The Cochrane analysis by Gøtzsche et al. showed that the efficacy of nystatin on fungal colonization in patients with severe immunodeficiency was not different from placebo.[3] In the prospective study of Egger et al., the use of nystatin in neutropenic cancer patients was not recommended.[4] Nystatin is generally well tolerated by patients. Allergic contact dermatitis, fixed drug erup-

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DOI: 10.37609/akya.4051.c4815

lian cell wall but is found in the fungal cell wall structure, causing the osmotic structure of the fungal cell to be disrupted. It has shown in vitro activity against many aspergillus and candida species. It is the first echinocandin approved by the FDA for the treatment of candidemia and esophageal candidiasis, empirical therapy in neutropenic patients with refractory fever, and salvage therapy of infections caused by Aspergillus species. It is administered intravenously because its oral absorption is low.[1,47] Mora-Duarte et al. found caspofungin to be more effective than amphotericin B and to have lower side effect rates in a randomized controlled study conducted with patients diagnosed with invasive candidiasis and candidemia.[48] Caspofungin is generally well tolerated. The most frequently reported adverse events during infusion are fever, chills, nausea, vomiting, abdominal pain, headache, diarrhea, phlebitis/thrombophlebitis, erythema, and skin rash. More rarely, life-threatening side effects such as pulmonary infiltration and anaphylaxis have been reported. Although transient elevations in ALT, AST, and ALP have been reported, there is no clinical evidence of hepatotoxicity. Leukopenia, elevated creatinine, hypokalemia, and hypercalcemia are other reported laboratory abnormalities.[48] Since caspofungin does not affect the CYP450 enzyme system, it causes fewer drug interactions than azole group drugs. In the geriatric population, the area under the curve (AUC) increases by approximately 30%, but no dose adjustment is reported.[49] Caspofungin has been shown to not alter plasma levels of cyclosporine. Caspofungin reduced the trough concentration of tacrolimus by 26% in healthy adults. Although standard monitoring is recommended, tacrolimus dose adjustment is recommended. It has been reported that co-administration of caspofungin with amphotericin B, mycophenolate mofetil, itraconazole and nelfinavir does not significantly alter caspofungin levels in healthy adults. Concomitant use of caspofungin with inducing agents such as efavirenz, rifampin, nevirapine, phenytoin, dexamethasone, and carbamazepine has been shown to result in a decrease in caspofungin AUC.[48,49]

Micafungin

Micafungin, like caspofungin, disrupts the structure of the fungal cell wall by blocking b-(1,3)-D-glucan synthase. It is administered intravenously due to its low oral absorption like caspofungin. Its in vitro activity against many Aspergillus and Candida species is similar to caspofungin. Indicated for candidiasis prophylaxis in patients undergoing esophageal candidiasis and hematopoietic stem cell transplantation. Like caspofungin, micafungin is poorly absorbed when administered orally; therefore, it is administered by intravenous infusion.[1,50] In a study conducted with 70 patients with deep mycosis, the response to treatment after micafungin treatment was determined as 57% in aspergillosis and 79% in candidiasis.[51] In a study conducted with 588 patients with candidemia and noncandidemic invasive fungal infections, treatment success in patients receiving 100 mg and 150 mg/day micafungin was found to be similar to caspofungin. No difference in the frequency of side effects was observed between the groups receiving micafungin and caspofungin.[52] The most frequently reported adverse effects of micafungin are nausea, vomiting, headache, diarrhea, abdominal pain, chills, fever, rash, leukopenia, anemia, and hypokalemia. Less frequently, dyspnea, tachycardia, hyperhidrosis, constipation, urticaria, erythema, and elevated liver function tests have been reported. Rarely, injection site phlebitis, thrombophlebitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported. Micafungin had no effect on the pharmacokinetics of cyclosporine, tacrolimus, prednisolone, mycophenolate mofetil, sirolimus, rifampin, nifedipine, fluconazole and ritonavir.[1,50–52]

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CHAPTER 36

CICLOSPORIN (Cyclosporine)

Suat SEZER [1]

INTRODUCTION

Cyclosporine was first isolated from Tolypoclodium inflammatum, a soil fungus in 1970. Cyclosporine, which initially had a narrow antifungal spectrum, was found to be a potent immunosuppressive drug in 1976 and was used to prevent transplant rejection in organ transplantations.[1] It was approved for use in the treatment of psoriasis by the United States Food and Drug Administration (FDA) in 1997. Although it was not approved by the FDA, cyclosporine was approved for the treatment of atopic dermatitis in other countries. Off-label, cyclosporine is among the treatment options for many skin diseases such as chronic spontaneous urticaria, alopecia areata, lichen planus, and pyoderma gangrenosum.[2]

PHARMACOLOGICAL CHARACTERISTICS STRUCTURE AND METABOLISM

Cyclosporine is a cyclic polypeptide immunosuppressive agent that consists of 11 amino acids. It forms a complex with cyclophilin, a cytoplasmic immunophilin.[3] Cyclosporine is a lipophilic molecule that is poorly absorbed after oral administration and highly variable individual bioavailability. Bile salts are needed to facilitate absorption, and maximum plasma concentration is reached in 2-3 hours. A hydrophilic microemulsion form was developed to increase oral bioavailability and reduce variations in absorption (Neoral). The bioavailability of the microemulsion form is greater than the oral form.[4] Topical cyclosporine penetrates poorly through intact skin and its use is ineffective.[5]

Cyclosporine dose should be divided into two doses a day and taken at the same time each day to minimize individual differences in serum concentration.6 Cyclosporine is available in emulsion capsule form (25 and 100 mg) or solution (100 mg/5 mL).7 The oral solution can be mixed with apple juice, orange juice, or milk.8 It is distributed widely in the body because of its lipophilic structure. Oral bioavailability is around 20-30% because of first-pass metabolism in the liver and enzymatic degradation in the small intestines.9 Its bioavailability and systemic clearance are controlled in the liver by cytochrome (CYP) 3A4 and CYP3A5, cytochrome P450 isoenzymes, and the P-glycoprotein pump and genetic variations cause individual differences in cyclosporine metabolism. The majority of its metabolites are excreted in the bile and only 6% are excreted in the urine. The half-life of cyclosporine in serum is 6-24 hours.4

MECHANISM OF ACTION

Cyclosporine becomes active after forming a complex with cyclophilins in the cytoplasm showing its main activity through the inhibition of T cell function. It

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DOI: 10.37609/akya.4051.c4816

be treated like patients with kidney failure.[36, 37] Since cyclosporine is a nephrotoxic drug and the risk of these side effects increases with aging, the long term use of cyclosporine should be paid attention. As a recommendation, its use in the elderly patients with atopic dermatitis should be no longer than 12 weeks and could be restarted intermittently after a break of at least 2 weeks.[38] Cyclosporine-induced hypertension is more common in elderly patients.[6] The risk of non-melanoma skin cancer increases with cyclosporine, and cases of lymphoma have also been reported. Cyclosporine should be used carefully due to the risk of carcinogenesis generally increases with aging.[38]

In conclusion, the use of cyclosporine in the geriatric population should be very carefully due to the increased risk of renal failure, cardiovascular comorbidities, polypharmacy and skin malignancy.[38, 39]

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CHAPTER 37

METHOTREXATE

Özge Sevil KARSTARLI BAKAY [1]

INTRODUCTION

In 1951, as a result of Gubner's observation that psoriasis lesions cleared rapidly in cancer patients treated with the anti-metabolic drug aminopterin Methotrexate (MTX), was developed as a less toxic and more stable form and began to be used in dermatology[1]. MTX is used in the treatment of many diseases such as psoriasis, atopic dermatitis, pityriasis rubra pilaris, lichen planus, autoimmune bullous diseases, lymphoproliferative diseases, granulomatous dermatitis, connective tissue diseases, vasculitides[2, 3]. The elderly population is gradually increasing and changes due to the aging process cause differences in the effectiveness of drugs and the frequency of side effects. Furthermore, the higher rate of multiple drug use in this group requires caution in terms of drug interactions. MTX is a treatment modality used for many diseases in terms of cost-effectiveness, and when preferred in the geriatric population, drug- and patient-related characteristics should be considered.

METHOTREXATE MECHANISM OF ACTION

MTX is effective in dermatological indications with its anti-inflammatory, anti-proliferative and immunosuppressive features. MTX terminates the activity of folinic acid by competitively inhibiting the enzyme dihydrofolate reductase. As a result, it inhibits the synthesis of deoxythymidylic acid, which plays a role in DNA formation[4]. Although inhibition of the folic acid pathway defines its role in the antineoplastic effects of MTX, its effect on inflammatory diseases is limited. It has been hypothesized that methotrexate exerts its anti-inflammatory effects primarily through inhibition of lymphocyte proliferation[5]. However, over time it has become clear that its anti-inflammatory effects are mainly related with its effects on adenosine[5-7]. MTX inhibits 5-aminoimidazole-4-carboxamide ribonucleotide (AICAR) transformylase (ATIC), which catalyzes one of the final steps of de novo purine synthesis. Inhibition of ATIC leads to increased AICAR levels, resulting in a net increase in intracellular and extracellular adenosine[5]. Adenosine is a purine nucleoside that is considered an endogenous anti-inflammatory combination. It has been shown to have potent and strong anti-inflammatory effects on many different target cells by binding to specific cell surface receptors. It inhibits the oxidative burst in neutrophils and monocytes, prevents leukocyte chemotaxis, and inhibits the secretion of multiple cytokines from monocytes and macrophages, including tumor necrosis factor-alpha, interleukin (IL)-10, and IL-12[2].

STRUCTURE AND METABOLISM

Methotrexate (4-amino-N10methyl pterogliglutamic acid) is a folic acid analog with a structure similar to folic acid. Irreversibly and competitively inhibits dihydrofolate reductase[5]. MTX can be administered

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DOI: 10.37609/akya.4051.c4817

ity needs to be considered. A sudden negative change in blood counts should alert to this possibility[13].

Patients should be evaluated for pulmonary toxicity in the presence of dry cough, fever or dyspnea. Baseline chest radiographs should be obtained to detect interstitial and alveolar infiltrates, hilar adenopathy, pleural effusions, and pulmonary fibrosis. MTX may also cause reactivation of latent tuberculosis in endemic countries, so tuberculosis screening is recommended in risk groups[19].

Methotrexate Use in Geriatric Population

Elderly patients are more likely to MTX side effects due to age-related failure in kidney and liver function. Additionally, MTX is transported in the bloodstream by binding to albumin and the free form is active. Therefore, decreased albumin concentration associated with malnutrition in the elderly may alter methotrexate activity[13]. Studies have reported that these risk factors in the geriatric patient population do not cause a negative effect on effectiveness. However, it is difficult to reach consensus on security-related data[20-24].

In a recent study, it was reported that all severe toxicity findings due to MTX over a 12-year period were observed in individuals over 70 years of age. In this study, the risk of MTX toxicity was significantly higher in patients over 70 years of age with low glomerular filtration rate, using diuretics, proton pump inhibitors and levetiracetam[20]. Another study concluded that the geriatric group differed little from other patients in terms of toxic side effects, but gastrointestinal and pulmonary problems were more common in older patients[23].

Advanced age is a risk factor for mortal complications such as pancytopenia and pancytopenia-related sepsis in patients using MTX[25]. On the other hand, studies evaluating the elderly patient group with rheumatoid arthritis reported that weekly low-dose MTX treatment is safe if hepatic and renal functions are carefully monitored[26]. Folic acid supplementation and close monitoring are recommended to reduce the risk of MTX toxicity in geriatric patients[13]. In addition to physiological changes in the geriatric group, multiple drug use and use of incorrect doses of MTX and other drugs due to impaired cognitive functions are other important risk factors for MTX toxicity[24, 27].

Vaccination is another important consideration in geriatric patients on MTX. MTX reduces the immunogenicity of the SARS-CoV-2 vaccine in an age-dependent manner. It has been shown that administering the drug at least 10 days after using MTX in patients over 60 years of age significantly improves the antibody response[28].

Consequently, MTX should be preferred in lower doses in geriatric patients. Its use should be avoided in patients with hypoalbuminemia, renal failure and possible drug interactions. Even if no condition is detected that prevents the use of the MTX, patients should be closely monitored, considering age-related physiological changes.

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CHAPTER 38

BIOLOGICS (Use of Biological Agents in the Geriatric Patient Population)

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INTRODUCTION

Advancements in the understanding of the pathophysiology of inflammatory skin diseases and drug development have led to the emergence of biological therapies in dermatology. Biological therapies are molecules that specifically target cytokines involved in immune-mediated diseases. In dermatology, both approved and emerging biological therapies act extracellularly to modulate T-cell activation and differentiation, block cytokines, or eliminate pathogenic B cells. Biological agents can be classified into three main groups: monoclonal antibodies, fusion proteins, and cytokines[1].

Depending on their mechanism of action, biological drugs have been utilized for various dermatological indications. Among the most used biological therapies are tumor necrosis factor-alpha (TNF-α) inhibitors (anti-TNF-α), interleukin (IL)-12/IL-23 inhibitors, IL-17 inhibitors, IL-23 inhibitors, rituximab, immunoglobulin E (IgE) antagonists, and dual IL-4/IL-13 inhibitors.

The World Health Organization (WHO) defines elderly individuals as those aged 65 years and older. This patient group differs from younger adults in several ways, particularly in terms of pharmacokinetic and pharmacodynamic changes. These changes are primarily attributed to altered distribution volumes (e.g., reduced muscle mass and increased body fat), decreased liver metabolism, and diminished kidney function[2]. Additionally, the immune system undergoes age-related changes, known as Immunosenescence. Immunosenescence refers to the gradual decline in both innate and adaptive immunity associated with aging. This chronic inflammatory state contributes to the increased susceptibility of elderly individuals to infectious diseases, as well as their predisposition to inflammation-related and autoimmune conditions.

PREPARATION FOR BIOLOGICAL AGENTS

Before initiating biological treatments, a detailed patient history should be obtained, and specific tests, such as HIV screening, hepatitis serology, tuberculosis screening, and pregnancy testing, should be conducted as appropriate for proper agent selection, similar to other populations [3]. According to current data and recommendations, patients receiving anti-TNF-α, IL-12/23 inhibitors, IL-17 inhibitors, IL-23 inhibitors, or CD20 antagonists should be considered immunosuppressed and vaccinated accordingly [4]. Patients with chronic inflammatory and autoimmune diseases are inherently more susceptible to severe in-

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and IgG levels should be monitored both before and during treatment [72].

CONCLUSIONS

The biologic agents (anti-TNF-α, anti-IL/12/23, anti-IL-27, and anti-IL-23) with which we have gained experience in the geriatric age group primarily treating moderate-to-severe psoriasis, while treatments with rituximab for pemphigus vulgaris, omalizumab for chronic urticaria, and dupilumab for atopic dermatitis have been introduced in recent years. Biologics should be preferred for the moderate-to-severe forms of these diseases when conventional systemic treatment agents are ineffective, contraindicated, or associated with severe side effects. Biologics used in the elderly population pose an increased risk of infection compared to younger patients or elderly individuals not receiving biologics. Their efficacy and safety were also widely reported during the SARS-CoV-2 pandemic [73]. Several global real-world studies have not indicated an increased likelihood of adverse reactions in geriatric psoriasis patients receiving biologic therapy.

The introduction of biologic drugs and small molecules has expanded treatment options for psoriasis, especially for elderly patients who are often undertreated for various reasons. Data on the efficacy and safety of these drugs in elderly individuals are gradually increasing. In this scenario, a personalized approach is needed to deliver the right drug to the right patient at the right time, to maximize clinical benefit without posing risk. Undoubtedly, broader prospective cohort studies are needed to evaluate the safety of biologics in the elderly [11].

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CHAPTER 39

SMALL MOLECULES

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INTRODUCTION

Small molecule inhibitors are chemically synthesized for specific purposes and target intracellular signaling molecules. They can be administered orally or topically.[1] Due to their small molecular size, these agents have high tissue penetration. They have shorter half-life and a faster onset of action than biologic treatments, which are another targeted treatment group. Small molecules also act on more than one cytokine.[2]

Biologics and small molecule inhibitors represent viable treatment alternatives for the geriatric patient group, where the use of classical treatments such as methotrexate and acitretin is limited due to contraindications or side effects. However, geriatric patients are frequently excluded from randomized controlled trials (RCTs) due to upper age limits, comorbidities that disproportionately affect older individuals, and polypharmacy. As a result, the efficacy and safety data for small molecules in elderly patients are limited, with the available data typically derived from small real-world studies.[3–5]

PHOSPHODIESTERASE-4 ENZYME INHIBITORS

Apremilast

Apremilast increases intracellular cyclic adenosine monophosphate levels by inhibiting the phosphodiesterase-4 (PDE-4) enzyme, which results in a reduction of cytokine levels, including TNF-alpha, IL-2, IL-8, IL-12, and IL-23. The US Food and Drug Administration (FDA) has approved this product for the treatment of psoriasis, psoriatic arthritis, and oral ulcers in Behcet's disease. Apremilast is also used off-label to treat a number of other dermatological conditions, including cutaneous sarcoidosis, lichen planus, atopic dermatitis (AD), chronic aphthous stomatitis, chronic actinic dermatitis, hidradenitis suppurativa, and discoid lupus erythematosus.[6,7]

While chronic infections, malignancy and lymphoproliferative diseases, being underweight, depression and advanced renal failure are considered relative contraindications to apremilast treatment, the most frequently reported side effects are gastrointestinal disorders, including vomiting, dyspepsia and abdominal pain, upper respiratory tract infections, insomnia, headache, depression and weight loss.[8] Apremilast represents a compelling treatment alternative for the geriatric patient subgroup, owing to a

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abolic syndrome, and a history of smoking, the use of JAK inhibitors should be reserved for cases where no other treatment alternatives are avaible.[32]

Herpes zoster

The risk of herpes zoster is increased under the treatment JAKi. The risk is further increased in geriatric age and in cases where concurrent therapy with other immunosuppressive agents such as systemic steroids is present.[23,29] Patients should be vaccinated against herpes zoster prior to initiating JAKi treatment.[29,33] If herpes zoster develops during JAK inhibitor treatment, the treatment should be discontinued until the patient has recovered.[26]

Gastrointestinal perforation

In consideration of the potential risks documented in clinical studies, it is important to bear in mind the possibility of gastrointestinal perforation especially in patients with a history of diverticulitis and those undergoing concomitant nonsteroidal anti-inflammatory drug or systemic glucocorticoid therapy.[26]

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CHAPTER 40
ULTRAVIOLET (UV), PHOTODYNAMIC THERAPY (PDT), AND ENERGY-BASED DEVICES (EBDS) IN THE GERIATRIC POPULATION

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PHOTOTHERAPY AND PHOTOCHEMOTHERAPY

Phototherapy refers to the use of non-ionizing radiation for the treatment of skin diseases and has a long-standing history in dermatological therapies. In 1903, Niels Finsen was awarded the Nobel Prize in Medicine for using light to treat a cutaneous mycobacterial disease. This achievement paved the way for the use of phototherapy in the treatment of skin diseases. In the mid-20th century, advancements in UV-B light therapy created new treatment options for conditions such as psoriasis. (1)

In the 1970s, photochemotherapy (PUVA), a combination of psoralen and UV-A radiation, was introduced and began to play a significant role in the treatment of skin diseases in the last quarter of the 20th century. In recent years, advancements such as narrowband UV-B therapy, laser treatment, targeted phototherapy, photodynamic therapy (PDT), and UV-A1 have revolutionized photodermatology. These innovations have enabled a more targeted and effective treatment of diseases. (1)

Phototherapy refers to the use of UV light in the treatment of skin diseases. The term phototherapy is used for treatments that utilize light at wavelengths of 311-313 nm (narrowband UVB) without the administration of photosensitizing agents, while the application of long-wavelength UVA light (320 nm-400 nm) to the patient following the systemic or topical use of the photosensitizer psoralen is referred to as PUVA (photochemotherapy). (2) Although phototherapy is an effective and reliable treatment method proven in the adult population, the literature on its use in the elderly population is insufficient. (3)

PHOTOTHERAPY IN THE ELDERLY

Phototherapy is a safe and generally recommended treatment method for elderly patients. However, its ability to reduce cardiovascular risks has not yet been established. There are several important considerations to take into account when evaluating the feasibility of this treatment method. It is important to consider the patient's ability to access the phototherapy center three times a week and any physical limitations that may hinder their ability to remain in the phototherapy booth. For example, elderly patients who must use a wheelchair may not be able to stand during the treatment. Therefore, their transport and coordination with caregivers are critically important for the effectiveness of the treatment. (4)

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CHAPTER 41

CRYOTHERAPY AND ELECTROCOTERISATION

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CRYOTHERAPY

Cryotherapy is the treatment of skin lesions through the application of a cryogen. In this procedure, liquid nitrogen is the most commonly used cryogen, released from the unit at -196 C and impacting the skin at approximately -70 C from a distance of 1-2 cm. Solid carbon dioxide and liquid nitrous oxide are other agents that can also be used. It exerts its effect by rapidly decreasing the temperature of the targeted tissue, resulting in cold injury. It primarily causes tissue damage through two mechanisms (1). The first mechanism is tissue ischemia caused by vascular endothelial damage. The other is necrosis that develops due to edema and cell rupture created by ice crystals formed during the freezing and thawing cycles.

Liquid nitrogen is stored in highly insulated long-term storage tanks and is transferred to a handheld device for use. There are various techniques for applying liquid nitrogen to a lesion. The main methods include open (spray), semi-open (cone), closed (probe), tweezers, cotton-tipped applicator, and intralesional techniques. The most appropriate technique should be selected based on the type, size, depth, and location of the lesion.

Indications

Cryotherapy is used in dermatology for the treatment of various skin lesions. Its key advantages include being safe, effective, simple, practical, low-cost, not requiring anesthesia, and achieving good cosmetic results. Benign lesions treated with cryotherapy include seborrheic keratosis, verruca, acrochordon, molluscum contagiosum, solar lentigo, sebaceous hyperplasia, keloid/hypertrophic scar, and dermatofibroma. While a single session is often sufficient, in cases where multiple sessions are needed, treatments can be repeated at intervals of 3-4 weeks. Among the premalignant lesions that increase with age are actinic keratosis, and among malignant lesions, basal cell carcinoma (BCC) and non-invasive squamous cell carcinoma (SCC) can also be treated with cryotherapy. Variable effectiveness and recurrence rates have been reported for the treatment of lentigo maligna (LM), which is associated with chronic sun exposure and is more frequently seen in older individuals (2). Cryotherapy is not the first choice for the treatment of malignant lesions of the skin. However, it should be noted that the inflammatory response generated against the antigens released from the cells destroyed by cryotherapy can create an anti-tumor immune response, providing an advantage over excisional surgery, especially for

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CONCLUSION

Cryotherapy and electrosurgery applications provide an effective alternative treatment option, especially for geriatric individuals who cannot tolerate surgery. A personalized approach is important in choosing the appropriate treatment. While these methods are effective, they should be applied carefully to minimize potential complications. The post-treatment follow-up process should be planned in the most suitable way for each patient.

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CHAPTER 42

DERMATOSURGERY

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GERIATRIC DERMATOSURGERY

Geriatric dermatologic surgery is a medical field that involves the surgical treatment of dermatological issues in older individuals. Dermatologic surgery encompasses all surgical procedures performed for diagnostic, therapeutic, cosmetic, and aesthetic reasons. The increase in life expectancy, along with the rising frequency of benign and malignant skin lesions associated with aging, has led to an increase in the number of patients seeking dermatologic surgery due to cosmetic expectations. An appropriate surgical approach is necessary, taking into account age-related skin changes in the geriatric population. In elderly individuals, factors such as frailty, cognitive impairment, comorbidities, and polypharmacy can pose several challenges in surgical treatment and management (1).

Geriatric 8 (G8) and Karnofsky Performance Scale (KPS) are assessment tools used to determine the overall health status and surgical risks of elderly patients. These are rapid and effective screening scales that can be utilized to assess frailty, particularly in the treatment planning for malignancies in geriatric dermatologic surgery. Frailty refers to a condition in which an individual's physical and functional reserves are diminished due to the aging process, making them more susceptible to various stress factors (1). It is estimated that frailty affects approximately 10-25% of individuals aged 65 and older (2). Clinicians use these screening tools to evaluate frailty and overall health status in elderly patients in outpatient settings, thereby determining their ability to tolerate invasive treatment procedures. In cases where the morbidity of treatment is expected to outweigh its benefits, minimal invasive treatment methods may be employed instead of the gold standard surgical treatment. However, in some instances, the need for continuity of treatment and prolonged wound care in frail individuals can complicate less invasive treatments due to the burden they impose. In such cases, a single-session curative treatment may be preferred, providing effective treatment that can enhance the patient's quality of life. Careful evaluation of treatment options and a personalized approach in elderly and low-functioning individuals are crucial for optimizing health outcomes (3,4).

Data regarding complications of dermatologic surgery in frail elderly patients is limited in the literature (5, 6, 7, 8, 9, 10). However, the existing data indicates that the risk of complications following any surgical intervention is high. Complications include bleeding, treatment burden such as post-operative care, increased mortality, infection, delayed healing, and functional decline. Addressing these risks through comprehensive preoperative evaluations, individualized treatment plans, and appropriate management strategies is essential to achieve the best outcomes in this vulnerable population.

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Electrodessication and curettage can be applied to small and superficial lesions. However, the inability to provide reliable margin control is a disadvantage, and it should not be preferred, especially in recurrent and high-risk tumors. In addition to being easily tolerated, postoperative wound care in elderly patients can negatively affect their quality of life (42).

Cryosurgery is another method that can be used in the treatment of well-defined, small, low-risk non-melanoma skin cancers. It may be preferred in elderly patients, particularly those with surgical contraindications or who cannot tolerate invasive procedures, due to its rapid and outpatient applicability, lack of anesthesia requirement, and ability to provide good aesthetic results. Since the healing process can be somewhat longer in elderly individuals, the patient and/or caregiver should be informed about wound care and follow-up. Additionally, greater caution should be exercised regarding damage to surrounding tissue in elderly individuals.

Intralesional chemotherapeutics can be used alone in tumors such as keratoacanthoma and SCC, or as neoadjuvant therapy to reduce tumor size preoperatively, thereby facilitating a simpler surgical approach (43). Methotrexate, 5-fluorouracil, interferon alpha, and bleomycin are effective chemotherapeutics. Literature reports cases of pancytopenia development following intralesional methotrexate application in dialysis-dependent patients, indicating that caution should be exercised, particularly in elderly patients (44).

Lasers target tumor components through ablative and non-ablative mechanisms. Particularly, carbon dioxide (CO2) and ND lasers have been found effective in the treatment of low-risk BCC, providing a comfortable treatment option for geriatric patients (45).

Radiation Therapy

In elderly patients where surgical treatment is not appropriate, radiation therapy can be used for the treatment of inoperable large BCC and SCC. It provides an important advantage as a tissue-preserving and non-invasive method. However, the cure rates are lower. Aesthetic results are generally poorer compared to surgical treatment, and possible side effects include erythema, edema, ulceration, radionecrosis, chronic dermatitis, and radiation-related malignancies.

Topical treatments, such as 5-fluorouracil and imiquimod, offer an effective and cosmetically satisfying option for superficial and early-stage skin malignancies. Both are approved for actinic keratosis and superficial BCC, but they are used off-label for the treatment of in situ SCC and lentigo maligna. In treating these lesions, the option of topical treatment provides a tolerable treatment possibility for elderly patients while avoiding aggressive treatment methods. Local reactions such as itching, burning, erythema, edema, pain, erosion, and irritation can limit the use of these treatments, especially for geriatric individuals, thus requiring careful information for the patient and/or their caregiver. Additionally, the high recurrence rates and the lengthy treatment process can pose disadvantages, particularly for elderly patients (38).

CONCLUSION

In geriatric dermatologic surgery, the decision for surgical intervention should be made considering the patient's overall health status, fragility, surgical tolerance, and treatment goals. In this process, non-surgical or minimally invasive approaches may be preferred initially. However, it is essential to develop a personalized treatment plan to maximize patient safety and the success of treatment outcomes.

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CHAPTER 43

VACCINATION AND SKIN TESTS (Vaccination & Skin Tests in the Elderly Population)

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INTRODUCTION

Vaccination is fundamentally defined as the administration of immunogenic contents derived from specific pathogens to the host to elicit an adequate immune response. Various vaccines are recommended to be administered in different age groups at varying doses and intervals in most countries. This approach significantly reduces the incidence of various infectious diseases such as influenza, pneumonia, and COVID-19, along with the severe clinical courses, hospitalizations, and complications, including death, associated with these diseases.

In a review by Ciarambino et al., it has been reported that aging leads to a decrease in naive T cells, T cell functions, B cell response, and antigen recognition. This decline in innate and adaptive immune system functions with aging is called immunosenescence. (1) These changes in immune cells in the elderly population result in a decreased response to vaccines.

Currently recommended vaccines for the elderly include Influenza, Pneumococcal, Herpes Zoster, and COVID-19 vaccines. (2)

INFLUENZA VACCINE

The elderly population is at high risk for influenza and its complications. Since its introduction, the influenza vaccine has targeted high-risk groups, such as elderly adults over 65 and those with underlying comorbidities.

In Turkey, four inactivated quadrivalent influenza vaccines were available for the 2020-2021 season. These included A/Guangdong-Maonan/SWL 1536/2019 (H1N1) pdm09-like virus, A/Hong Kong/2671/2019 (H3N2)-like virus, B/Washington/02/2019 (B/Victoria lineage)-like virus, and B/Phuket/3073/2013 (B/Yamagata lineage)-like virus. (3)

Local and systemic side effects can be observed after influenza vaccination, usually within the first seven days. Systemic side effects include fever, headache, fatigue, nausea, and rash. Local side effects include tenderness, erythema, induration, and hardness at the injection site. These side effects typically resolve within a few days. However, more severe side effects mediated by T cells and the complement system can occur. (4)

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DOI: 10.37609/akya.4051.c4823

In the elderly population, a decrease in response to allergens in prick tests has been reported. This is explained in the literature by reducing allergy prevalence and skin test reactivity with age. (42, 43)

Due to aging and photodamage exposure, there is a decrease in the number and function of mast cells in the skin. Additionally, the elderly often use multiple medications, such as antihistamines and tricyclic antidepressants. These factors affect the prick test results in the geriatric population. (40)

Considering these factors, King and colleagues (40) have developed recommendations for prick testing in the elderly:

1. Before testing, the skin area to be tested should be examined for atrophic or photo-induced changes.
2. If signs of skin atrophy/photoaging are detected, a sun-protected skin area, such as the lower back, should be used for testing.
3. If a suitable skin area cannot be determined, in vitro allergen testing should be considered.
4. A standard allergen test should always include a histamine control. The intensity of the skin reaction is expressed as the ratio between allergen-induced and histamine-induced wheals. This accounts for the generally reduced skin reactivity to allergens in the elderly.
5. When a positive reaction to an allergen is detected, it should be correlated with the patient's history of exacerbation. Ideally, a provocation test should be conducted to confirm the actual allergy.
6. Based on identifying specific allergens the patient is sensitive to, avoidance measures or specific allergen vaccinations may be recommended.

PATCH TEST

Contact dermatitis (CD) is a dermatological condition characterized by inflammation resulting from direct contact with a chemical substance on the skin. Contact dermatitis is classified into irritant (ICD) and allergic (ACD) based on different pathogeneses, with ICD accounting for approximately 80% of cases. (44)

Aging leads to xerosis, impairment of the epidermal barrier, delayed healing, and reduced epidermal lipid synthesis in the skin. These factors increase the risk of both ICD and ACD. (45) In contrast, aging is associated with decreased epidermal Langerhans cell density, which is linked to reduced reactivity to various allergens. However, prolonged and increased exposure to potential sensitizing agents over the years is associated with an increased risk of ACD. (46)

The patch test is a diagnostic test for Type 4a allergic reactions, demonstrating the presence of specific T lymphocytes developed against contact allergens. It is used in dermatology practice to diagnose ACD, systemic allergic dermatitis, photoallergic contact dermatitis, and drug eruptions.

The patch test is typically applied to the upper half of the back. The test site remains covered for 48 hours. Initial evaluation occurs at 48 hours, followed by assessments at 72 and 96 hours and on the 7th day. (47)

Piaserico et al. recommend re-evaluating the patch test in the geriatric population on the 7th day and considering weak reactions as positive. (48)

Among the most frequently detected allergens in patch tests in elderly patients are nickel and components related to topical medications (fragrances, preservatives, antibacterials, emulsifying agents). The high prevalence of nickel sensitivity can be attributed to sensitization at a younger age and long-term exposure. Positivity related to topical medications is associated with frequent and prolonged exposure to these substances. The literature reports that, in the geriatric population, the most common allergens responsible for ACD include fragrance mix, Balsam of Peru, neomycin, gentamicin, and lanolin. (49, 50)

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CHAPTER 44

NUTRITIONAL SKIN DISEASES

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INTRODUCTION

Nutritional diseases or malnutrition are disorders of body structure and function caused by an imbalance of energy, protein and other nutrients.[1] Malnutrition encompasses undernutrition or overnutrition, but is often used synonymously with "undernutrition". In a meta-analysis of 583,972 adults aged 65 years and older, malnutrition was found in 8.5% of community settings older adults, 28% of hospitalized and 17% of residential care older adults. The prevalence is higher in adults over 80 years of age ($p < 0.0001$), women ($p = 0.03$) and patients with one or more comorbidities ($p < 0.0001$).[2] Malnutrition is more common in older individuals due to chewing and swallowing problems, loss of limb function, limited movement, cognitive impairment, depressed mood, social isolation, acute and chronic diseases and restricted diets. Malnutrition is evaluated by clinical findings, laboratory parameters, anthropometric measurements and some screening tests. According to the American Society for Parenteral and Enteral Nutrition (ASPEN) 2012 criteria, malnutrition is diagnosed with the presence of 2 or more of the following criteria: inadequate energy intake; weight loss; loss of muscle mass; loss of subcutaneous adipose tissue; localized or generalized edema that may mask weight loss; and decreased functional status as measured by hand grip strength.[3] According to the criteria established by the Global Leadership Initiative on Malnutrition (GLIM), the diagnosis is based on the presence of at least one phenotypic (involuntary weight loss, low body mass index) or decreased muscle mass) and one etiologic criterion (decreased food intake or absorption due to acute/chronic illness, injury or inflammation).[4]

The clinical presentation of nutritional dermatoses often overlaps. Therefore, when evaluating nutritional deficiencies, a complete metabolic panel, complete blood count and inflammatory markers should be performed, as well as tests for suspected and comorbid nutrient deficiencies. Nutritional deficiencies can aggravate many skin diseases; in this chapter, only mucocutaneous manifestations primarily associated with nutritional deficiencies will be discussed.

MACRONUTRIENT DEFICIENCIES

Protein-Energy Malnutrition

Historically, protein-energy malnutrition (PEM) has been classified as marasmus and kwashiorkor. Marasmus occurs during periods of chronic starvation characterised by inadequate protein and calorie intake; kwashiorkor occurs as a result of prolonged inadequate protein intake. In modern terminology, marasmus refers to starvation associated with social or environmental conditions, whereas kwashiorkor is associated with chronic disease and inflammation

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DOI: 10.37609/akya.4051.c4824

intake, malignancy especially colon cancer, gastrointestinal surgery, chronic heart failure and bleeding. Tannate (tea), phosphates, phytate (in whole grains and seeds) and calcium-rich foods can impair iron absorption. Coilonychia, brittle nails, telogen effluvium, graying of hair, atrophic glossitis, angular cheilitis, stomatodynia, pallor of mucous membranes and skin, xerosis, generalized pruritus may be observed in iron deficiency. Other findings include hypochrome microcytic anemia, fatigue, decreased cognitive function, effort dyspnea, tachycardia, pica, dysphagia.

Serum iron level, total iron binding capacity, transferrin, transferrin saturation and serum ferritin levels are used to detect iron deficiency in patients with hypochromic microcytic anemia.[24] It should be kept in mind that transferrin and serum iron levels may decrease and ferritin levels may increase in inflammatory reactions.

The first line of iron deficiency treatment is oral preparations; ferrous sulfate is most commonly used, but ferrous gluconate and ferrous fumarate can also be used. For adults, 100-200 mg of elemental iron is recommended to be taken with vitamin C.[54] Replenishment of iron stores and normalization of serum ferritin usually occurs within 3-6 months after treatment. If no response is obtained with oral iron therapy, parenteral forms can be switched.

OTHER VITAMIN DEFICIENCIES16

- **Vitamin E Deficiency:** Impaired wound healing and immune function, seborrheic dermatitis-like rash.
- **Vitamin K Deficiency:** Hemorrhage-ecchymosis-purpura-like bleeding disorders.
- **Vitamin D Deficiency:** Although the skin is involved in vitamin D synthesis, there are no specific cutaneous manifestations associated with deficiency.
- **Vitamin B5 (Pantothenic acid) Deficiency:** Acomotrichia, burning foot syndrome.[55]

Conclusion

Considering the prolonged life expectancy and the high prevalence of malnutrition, alcohol and substance abuse, the awareness of dermatologists is important for early diagnosis of nutritional deficiencies and reduction of morbidity. In this spectrum of diseases, which often develop as combined deficiencies and may overlap clinically, history, physical examination and diagnostic tests will help in the diagnosis of the underlying deficiency(s). Although skin manifestations regress rapidly after treatment, patients should be followed up at regular intervals depending on the underlying cause.

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CHAPTER 45

SKIN PROBLEMS IN ALZHEIMER DISEASE, DEMENTIA AND OTHER CEREBROVASCULAR PROBLEMS

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INTRODUCTION

Dementia is a neurological disease characterized by progressive cognitive dysfunction and its incidence is increasing in the elderly. Although the pathogenesis is not fully understood, various genetic and environmental risk factors have been identified. The most common subtype of dementia is Alzheimer's disease, which constitutes approximately half of dementia cases. In Alzheimer's disease, there is pathological accumulation of amyloid-β and tau in the brain.[1]

Several studies have shown a correlation between Alzheimer's disease and certain skin conditions. In patients with Alzheimer's disease, the physiology of the skin is altered, and proteins such as amyloid beta and alpha-synuclein, which are associated with neurodegenerative diseases, are also deposited in the skin.[2,3] It is also known that the skin and the brain develop from the same ectoderm.[3,4] The relationship between Alzheimer's disease and autoimmune bullous diseases has been most frequently studied issue, and has been showed that the risk of developing bullous pemphigoid is 2.6 times higher in Alzheimer's patients. 5 The other study conducted in 2013 found that non-melanoma skin cancer is associated with a reduced risk of Alzheimer's disease.[6]

In this section, the relationship between dementia, Alzheimer's disease and other cerebrovascular diseases and skin diseases such as bullous pemphigoid, hidradenitis suppurativa, psoriasis, skin cancers and cutaneous amyloidosis will be discussed.

BULLOUS PEMPHIGOID

Bullous pemphigoid (BP) is an autoimmune skin disease characterized by subepidermal blisters on normal or erythematous background.[7] It is a rare and frequently occurs in the elderly, its incidence is increasing. 8 BP patients often have comorbidities such as cardiovascular diseases, diabetes mellitus, neurological disorders, psychiatric conditions, and malignancies, with the strongest association has been found between BP and neurological diseases. [9] A recent meta-analysis revealed that bullous pemphigoid increases the risk of dementia (RR=4.46), stroke (RR=2.68), epilepsy (RR=2.98), and multiple sclerosis (RR=12.40). 10 Additionally, existing neurological disorders may increase the risk of BP. One study found that most patients were diagnosed with at least one neurological disorder prior to BP, with neurological disease mean duration of 5.5 years. 11 No significant differences in clinical presentation, disease severity, and autoantibody response were observed between BP patients with and without neurological disorders. [12]

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DOI: 10.37609/akya.4051.c4825

Reflex sympathetic dystrophy is a syndrome characterized by pain that is disproportionate to the severity of an injury. This syndrome is accompanied by various dermatological findings such as edema, erythema, pallor, cyanosis, hypo- and hypertrichosis, hypo- and hyperhidrosis, blistering, onychodystrophy, white nails, ridging and ulceration.[40]

Unilateral pruritus has been reported as a complication of unilateral pontine infarction. Trigeminal trophic syndrome, a rare cause of facial ulceration, has also been described following ischemic infarction. Hyperhidrosis resulting from cerebral infarction has rarely been reported in the existing stroke-related literature, and its pathophysiological mechanisms and clinical significance remain unclear. Hyperhidrosis typically involves the face and arm and is transient, lasting from 2 days to 2 months. No association has been observed with Horner's syndrome, hypothalamic dysfunction, or any other autonomic dysfunction.[40]

In patients with hemiplegia, nail pathology presents in three main patterns: longitudinal reddish streaks, Neapolitan nails, and unilateral clubbing. Hemiplegia precedes nail damage by approximately 40 months. Unilateral pterygium inversum unguis is a nail abnormality resulting from the distal side of the nail bed/hyponychium adhering to the ventral surface of the nail plate, leading to obliteration of the distal groove.[40]

CONCLUSION

Bullous pemphigoid and psoriasis may increase the risk of Alzheimer's disease and dementia, while skin cancer may have a protective effect against Alzheimer's disease. However, the relationship between hidradenitis suppurativa, cutaneous amyloidosis, and Alzheimer's disease remains uncertain. Further studies are needed to better understand the connection between dementia, Alzheimer's disease, and dermatological conditions and to explore the underlying mechanisms.

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CHAPTER 46

DRUG METABOLISM IN GERIATRIC GROUP

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INTRODUCTION

Aging is an inevitable physiological process in higher organisms, which many biological functions are deteriorated in this or in that way. At the end, every living organism will die even though there is a chance to slow down of senescence or postpone its associated complications yet for a certain period of time. It has been estimated that a human being has the potential of 120-150 years of longevity.[1] although we has benefitted from this potential just a little bit more than a half of it thanks to modern medicines, improved sanitation and medical and healthcare in developed countries.[2]

Epidemiological data has revealed that the incidence of many age-related complications increase, e.g., decreased visual acuity, hearing loss, decreased muscle mass and strength, increased fat, immunosenescence, and disruption of cardiovascular homeostasis. On the other hand, increased cerebrovascular and neurological events such as stroke, dementia, Parkinson's etc., and metabolic diseases such as diabetes and metabolic syndrome are also seen.[3]

Elderly patients are liable to polypharmacy (use of multiple drugs) in order to control concomitant complications that increase with age. In this case, they may become particularly sensitive to the effects of the drug. At the same time, since the function of the elimination organs (e.g., the liver and kidneys) may be weakened, the accumulation of drugs in the body may inevitably occur. In this respect, drug metabolism and excretion issues in elderly patients should be well known and managed. While the metabolism of drugs is generally carried out in the liver, other tissues and organs may also contribute to the metabolism, depending on the drugs.

THE ORGANS PLAYING A ROLE IN DRUG METABOLISM

Our body is sensitive to liposoluble compounds. That's why our cells are naturally designed to render them from liposoluble forms to water-soluble forms so that they could be readily transferred to water compartments and could be excreted from the body as much as possible. For this purpose, it is vital that metabolic and elimination organs are fuctional. However, in the early and late stages of life, namely infancy and old age, these systems are either not fully developed or their functions are inadequate.

The most important organ in drug metabolism is the liver that has abundantly metabolizing enzymes the majority of which are cytochrome P_{450} enzymes (briefly named as *CYP*). CYP has several izozymes but

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considered to have a favorable safety profile and to be a safe option for elderly patients. It has few drug interactions, does not increase the risk of tuberculosis, and does not require laboratory monitoring, which provides advantages for elderly patients.[46]

In conclusion, apremilast appears to be a generally safe and effective treatment option in elderly patients. However, an individualized approach, especially with respect to renal function, should be adopted and further research should be conducted on long-term safety and efficacy.

JAK/STAT INHIBITORS (JAKINIBS)

The JAK/STAT signaling pathway plays an important role in the pathogenesis of various autoimmune and inflammatory diseases (such as rheumatoid arthritis, psoriasis, and inflammatory bowel disease).[47,48] Many cytokines exert their physiological, pharmacological and pathological effects through this signaling pathway.[49] In recent years, JAK inhibitors (*Jakinibs*) have shown promise in the treatment of many autoimmune diseases. For example, the first jakinib, tofacitinib, has received FDA approval for the treatment of rheumatoid arthritis.[49] Studies on how the metabolism of jakinibs changes in the elderly are insufficient. Furthermore, the available data also seem to be contradictory. For example, in an open-label phase I study with filgotinib, no change in the pharmacokinetics of the drug was observed in elderly individuals (65-74 and ≥75 years of age).[50] However, a slight increase in the $AUC_{0\text{-}24h}$ value of filgotinib was observed in those over 75 years of age, while there was no change in other pharmacokinetic parameters (Cmax, $t_{½}$, λ_z and Ae). Metabolite exposure was also increased in elderly subjects, but no change in metabolite formation and elimination was observed.

As a result, it was concluded that age did not have a significant effect on filgotinib and its metabolites.[50] It should also be noted that drugs such as baricitinib, which is metabolized in the liver but excreted largely unchanged via the kidneys, or tofacitinib and ruxolitinib, which are also excreted via the kidneys, should be closely monitored in elderly patients with reduced glomerular filtration rates due to potential drug accumulation.[51] In addition, it has been found that the side effect profile of JAK inhibitors differs in elderly patients compared to younger patients. Clinical studies have shown that serious side effects and conditions leading to treatment discontinuation are more common in elderly patients.

Specific side effects, especially thrombocytopenia, lymphopenia, and opportunistic infections, have been reported more commonly in the elderly population. In addition, the risk of major side effects, such as cardiovascular events, cancer, and serious infections, is also increased in elderly patients.[52] These differences also suggest that older individuals may be more sensitive to the metabolism and pharmacodynamics of JAK inhibitors. The increasing prevalence of comorbidities and polypharmacy with age may further complicate this situation. Therefore, a more cautious approach should be adopted when starting or continuing JAK inhibitor therapy in older patients, dose adjustments should be made, and patients should be monitored more closely for side effects.[52]

In conclusion, the side effect profile of JAK inhibitors in elderly patients differs significantly compared to young adults. These differences may be due to changes in drug pharmacodynamics with aging, as well as changes in drug metabolism. Therefore, the use of JAK inhibitors in elderly patients should be carefully evaluated and an individualized treatment approach should be adopted.

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CHAPTER 47

GERIATRIC PHARMACOTHERAPY IN DERMATOLOGY AND ADVERCE DRUG INTERACTIONS

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PHARMACOKINETICS IN THE ELDERLY

Medication Absorption: Although aging leads to a reduction in small-bowel surface area, slower gastric emptying, and an increase in gastric pH, these changes generally have minimal clinical impact on the absorption of most drugs (5). However, it should be kept in mind that there may be conditions such as atrophic gastritis and previous gastrointestinal surgeries in the elderly that can significantly affect drug absorption.

Volume of Distribution: As people age, body fat tends to increase while total body water decreases, affecting the distribution and elimination of medications. Lipophilic drugs, which are absorbed into fat tissue, may have a prolonged half-life and increased risk of side effects due to this increased fat volume. Additionally, aging leads to decreased serum albumin and increased alpha 1-acid glycoprotein levels, which can alter drug binding and efficacy (3,6). In cases of acute illness or malnutrition, reduced serum albumin can elevate the levels of free, unbound drugs, increasing the risk of toxicity for drugs. Thus, the volume of distribution (Vd) for medications changes with age due to shifts in body composition and plasma protein levels, potentially resulting in unexpected drug effects, especially in frail elderly individuals (7).

Hepatic Metabolism: There are two main stages of drug metabolism in the liver: Phase I (e.g. hydroxylation, oxidation, alkylation and reduction) and Phase II. Phase I reactions are affected by aging (3). Age-related decline in the clearance of medicines metabolized by cytochrome (CYP) enzymes in the liver has been observed, with preclinical studies showing a 37-60% reduction in CYP-dependent drug metabolism in elderly rats (8). Phase II reactions, including conjugation and glucuronidation, are less affected by age (9). Aging also diminishes first-pass metabolism, which can result in higher drug concentrations and increased risk of toxicity for some drugs. Additional factors such as smoking, decreased hepatic blood flow, and interactions with other drugs can further impact hepatic metabolism.

Decrease in renal function: As people age, their glomerular filtration rate (GFR) decreases, leading to reduced kidney function. Starting around age 40, the GFR declines by about 8 ml/min. This decline accelerates after the age of 65-70 (10). Serum creatinine and blood urea nitrogen (BUN) have traditionally been used as markers of renal function, but they are often inaccurate in older adults due to decreased muscle mass and creatinine production. As a result, older patients may have normal serum creatinine levels

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CHAPTER 48

GERIATRIC DERMATOPATHOLOGY AND IMMUNOPATHOLOGY

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INTRODUCTION

What constitutes old age and which subgroup is defined as "Elderly" is an arbitrary classification, and the age limit for this classification is gradually increasing. In practice, a chronological age over 65 is currently considered geriatric; however, this may change as average life expectancy increases.

Our skin, on the other hand, is a barrier organ exposed to environmental and chronological aging, which weaken its structure and functions. It is in constant contact with the body's external environment and therefore serves as the first line of defense against environmental threats (1). It primarily prevents water and electrolyte loss, the penetration of chemical substances, and plays a role in protecting against pathogenic microorganisms (2). The skin's barrier function, elasticity, resistance properties, and vascular reactivity show changes with aging in the epidermal, dermal, and vascular compartments (1).

SKIN HISTOLOGY

Histologically, the skin consists of 3 layers: Epidermis, dermis, and hypodermis. The architectural structural features of the skin, such as epidermal-dermal thickness, the distribution of skin appendages, and the amount of melanocytes show regional differences (2). Embryologically, the epidermis and skin appendages develop from the surface ectoderm, while the dermis and hypodermis develop from the mesoderm (2). The epidermis is composed of continuously renewing stratified squamous epithelium. The main cell of the epidermis, constituting approximately 95%, is the keratinocyte. As keratinocytes progress from the basal membrane towards the skin surface, they form morphologically distinct epidermal layers: stratum basale (or stratum germinativum), stratum spinosum, stratum granulosum, and stratum corneum. On the palms and soles, an additional layer, the stratum lucidum, is also found between the stratum corneum and stratum granulosum. The epidermis also contains melanocytes, Langerhans cells, and Merkel cells (2). The epidermis is a dynamic system whose metabolic activity is largely regulated by the integrity of the permeability barrier. This barrier is responsible for maintaining the balance between clinically normal and dry skin (3). Ensuring this balance is the task of the stratum corneum. The stratum corneum has a composition of 60% structural protein, 20% water, and 20% lipid. The integrity of the stratum corneum depends on its lipid composition, primarily including cholesterol, ceramides, and free fatty acids (3, 4). When the skin's moisture content falls below 10%, it is clinically

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CHAPTER 49

GERIATRIC DERMOSCOPY

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INTRODUCTION

The skin health of the elderly is an important part of their general health. The skin is the largest organ, covering the entire surface of the body and undergoes morphological changes during the aging process depending on intrinsic and extrinsic factors. Monitoring and management of these changes are critical to prevent complications. Dermoscopy is a noninvasive imaging technique used to diagnose changes in the skin and dermatological diseases. Dermoscopy and developing artificial intelligence (AI) applications offer new opportunities to serve this purpose (1,2). In this chapter, the skin characteristics of elderly and their differences from normal adults, common skin problems, the role of dermoscopy and the potential use of AI in these areas will be discussed.

SKIN AGING

There are several physiological, structural and biochemical changes in the aging skin. In addition, there are some changes in neurosensory perception, permeability, repair capacity and response to injury of skin (3). These changes lead to increase in the incidence of various skin diseases in elderly. Here, there are physiological changes seen in the aged skin:

Epidermal thinning: Epidermis layer becomes thinner and more sensitive with aging.

Flattening of the dermoepidermal junction: Reduction in dermal papillae causes flattening of dermoepidermal junction. That eventually leads to increased susceptibility to damage and an increased risk of dermoepidermal separation.

Decrease in collagen and elastin fibers: Decrease in collagen and elastin fibers in the dermis causes skin to lose its elasticity and firmness.

Loss of subcutaneous fat: Thinning of the fat layer under the skin causes skin to appear wrinkled.

Decreased blood circulation: Impaired blood vessel function slows down the healing process in the skin.

Decreased humidity: Decreased sweat gland production causes the skin to dry out.

GERIATRIC DERMOSCOPY APPLICATIONS

Dermoscopy is a non-invasive imaging technique used to examine skin lesions. During this procedure, a special tool, called dermoscope is used to observe the structures on the skin better. Dermoscope provides magnification on the lesions, allowing microscopic features to be observed. Dermoscopy applications,

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DOI: 10.37609/akya.4051.c4829

not sufficient to make a distinction. Therefore, histopathological examination is required.

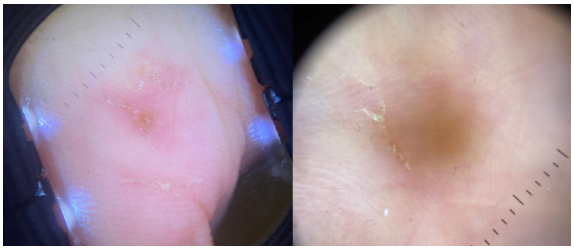

Figure 12. Scabies tunnels.

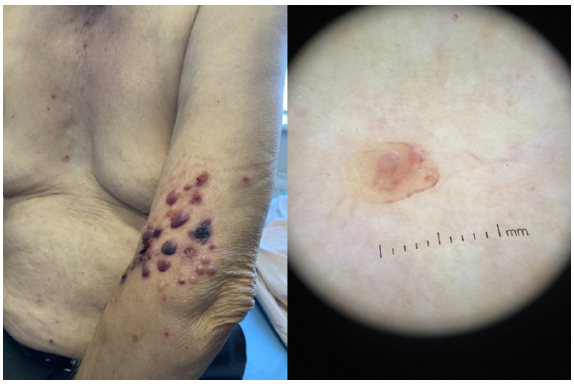

Figure 13 a. Bullous pemphigoid. **b.** Blister with erythematous and yellowish translucent base and regular borders.

FUTURE DIRECTIONS

Elderly patients may not be able to go to the hospital due to their systemic diseases or difficulties in accessing healthcare services. So that, they cannot comply with the determined follow-up periods in cases requiring close monitoring. For this reason, diagnosis and treatment are delayed in many skin diseases, especially malignant skin lesions, which are increasingly common in the elderly. In order to prevent this, teledermatology, which has become increasingly popular especially during the COVID-19 pandemic, comes to mind. Teledermatology allows remote diagnosis, close monitoring and cost and time savings by evaluating patients' skin problems through digital devices without having to meet with a dermatologist face to face. With increasing technology, there may be an increase in the efficiency that can be obtained from teledermatology. In the future, the digitalization of dermoscopy, the integration of remote assessment and AI applications can make the diagnosis process of skin lesions more accurate and efficient. For this, AI-supported systems need to be established. In order to establish these systems, a large database is needed first. AI can perform dermoscopic analysis using this large database. When creating a database, each data must be labeled by expert dermatologists and the images must be standardized. After the database is created, the data should be processed by AI using deep learning algorithms and the AI model should be tested for fine learning and model accuracy and sensitivity. If the AI models are integrated with teledermatology, risk assessment can be made for the lesions of elderly patients, possible skin diseases can be detected remotely and diseases can be followed closely. This can support dermatologists in the decision-making process.

CONCLUSION

Common skin lesions in elderly and the dermoscopic findings of these lesions are discussed in this chapter. As mentioned above, most of these lesions are clinically similar. Some specific findings seen in dermoscopic examination may guide the physician in distinguishing these lesions from each other. Thus, benign lesions can be separated from malignant lesions and unnecessary excisions can be prevented. Similarly, potential malignant lesions can be closely monitored by separating them from benign lesions, early diagnosis can be made and excisions can be made with appropriate surgical margins when necessary, thus decreasing the morbidity (cosmetics, etc.) and mortality rates due to skin malignancies in the elderly.

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CHAPTER 50

GERIATRIC PSYCHODERMATOLOGY APPROACHES

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Aslı AKSU [2]

INTRODUCTION

Psychodermatology is a subspecialty of dermatology that focuses on the relationship between the brain, immune system, cutaneous nerves, and the skin. Beyond the fact that the nervous system and the epidermis share the same embryonic origin, which is 'the ectoderm', the role of psychoneuroimmunology in the emergence of psychocutaneous disorders and psychosocial effects of skin diseases has gained interest, lately (1). A new classification of psychodermatological diseases, built and approved by experts and task forces in the field of psychodermatology, has recently been published. According to this classification, two main categories are presented; a main group related to primary mental health disorders affecting the skin and another main group related to primary skin disorders linked with mental health. Subsequently, these are divided into subgroups, taking into account the presence of visible skin lesions (primary or secondary) and psychopathological similarities (2). The connection between the mind and skin is complex and multidimensional, thus psychodermatology focuses on understanding this interaction and aims to help patients address and manage physical distress, depression, anxiety or other psychiatric comorbidities associated with the skin diseases by using both psychopharmacological and psychological interventions (3). Managing psychodermatological diseases in the geriatric population may be more challenging given the high rates of multiple comorbidities, particularly psychiatric and neurological comorbidities, along with polypharmacology and drug interactions, and the physiological changes in aging skin (4-6).

Both intrinsic and extrinsic changes in the skin in elderly lead to a wide variety of dermatological disorders. Factors such as systemic diseases, psychosocial status, personal habits, drug use, socioeconomic status, gender, nutrition, personal hygiene also contribute to the emergence of cutaneous conditions in older patients. Xerosis and chronic pruritus are among the most common dermatological conditions affecting the elderly. Systemic disorders such as liver disease, chronic kidney disease, thyroid disorders, hematological diseases and malignancies have been implicated in 10-50% of geriatric patients with chronic pruritus (7). Also, inflammatory skin diseases such as eczema, psoriasis, urticaria, or cutaneous lymphomas may be the cause of senile pruritus. The presence of primary skin lesions helps to distinguish pruritus associated with dermatological diseases. Though invisible mycosis fungoides or prebullous stage of bullous pemphigoid should be kept in mind (8-10). Psychogenic pruritus is most commonly reported among patients with depression and anxiety. Also, chronic pruritus significantly affects the quality of life and reduced quality of

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DOI: 10.37609/akya.4051.c4830

Neurotic excoriation, also referred as pathological skin picking disorder is included in the obsessive compulsive disorder and other related disorders section in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders of the American Psychiatric Association (DSM 5). Most common associated disorders are trichotillomania, nail biting, depression and obsessive compulsive disorders. Symptomatic treatment with cognitive behavioral therapy and psychopharmacological agents have been used with variable success, thus it is recommended to assess these patients in psychiatry-dermatology liaison clinics (7, 28). Another systematic review of N-acetylcysteine (NAC) treatment, showed favorable evidence for the use of NAC in several psychiatric and neurological disorders, particularly autism, Alzheimer's disease, depression, trichotillomania, nail biting, skin picking, obsessive-compulsive disorder. Considering the neurological comorbidities in the elderly, NAC may be a safe and effective choice of treatment in this population (29). Scalp dysesthesia is another psychodermatoses with an abnormal burning or itching sensation of the scalp in the absence of a cutaneous disease, usually related to neurogenic or psychogenic causes. It is also more common in the elderly, particularly in females, patients with diabetes mellitus and patients with psychiatric history (30).

Apart from the primary psychodermatoses, a study that included 310 geriatric dermatology patients, found that 45.5% of patients were depressed, 43.2% had anxiety, 20.3% had high stress and 11% had extremely large effect on dermatology life quality index (DLQI) (31). Consequently, a special attention to psychiatric comorbidities in the geriatric population is essential.

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CHAPTER 51

FUTURE OF GERIATRIC DERMATOLOGIC THERAPY

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AGING POPULATION

The rapid increase in the world population, especially after World War II, coupled with advancements in medicine, has led to a significant rise in the geriatric population.This is a reality that will become more pronounced in the coming years. By 2030, it is expected that 1.4 billion people will be aged 60 and above, with this number reaching 2.1 billion by 2050. In contrast, the population of children aged 0-9, which stood at 1.2 billion in 2000, is only projected to increase to 1.4 billion by 2050. This suggests that our future will be dominated more by the elderly than by children. (**Table 1**)[1]

Particularly in developed countries, where birth and death rates are rapidly declining, the elderly population will be felt much more acutely (**Table 2**). This situation will not only increase the workload for medical doctors but will also require those in many other sectors to become more knowledgeable and attentive as they provide the necessary services and care for this demographic.[2]

The rapid increase in the geriatric population will challenge some of the medical and non-medical truths we currently hold. The knowledge we have accumulated regarding pediatric care may become less relevant, while the information related to the care of the elderly, of which we currently have limited understanding, will be increasingly utilized. In addition to the knowledge and care burden, this demographic shift will also have financial implications. The market size for geriatric services, currently estimated at $1.45 trillion, is projected to grow to $2.88 trillion by 2032. Moreover, the fields necessary for the care of the geriatric population are underdeveloped in many countries. In countries where these fields are developed, the proportion of young people capable of maintaining this workforce is rapidly declining (**Figure 1**).[3] While it might be assumed that an increase in the young population is needed to match the rise in the elderly population for sustainability, the fact that the world has already exceeded its sustainable human population size presents another dilemma. From a comprehensive perspective, the world does not seem prepared for the aging population.

Furthermore, it is not just the increase in the population over 60 years of age that presents a problem. The life expectancy after 60 is also expected to reach 30 years by 2050.[1] This implies that these individuals may require an average of 20 years of care after their retirement. This situation suggests that a 28-year-old specialist today will be treating a specific generation

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DOI: 10.37609/akya.4051.c4831

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CHAPTER 52
IMPROVING TREATMENT ADHERENCE IN GERIATRIC DERMATOLOGY: CHALLENGES AND PRACTICAL STRATEGIES

Belma TÜRSEN [1]

INTRODUCTION

Treatment adherence is an important issue for successful dermatological care especially in the geriatric society. Older people often experience chronic and relapsing disorders such as eczema, pruritus, psoriasis, venous ulcers, xerosis, skin infections, autoimmune blistering diseases and skin cancers which require long-term managements. Due to age-related factors coherence to dermatologic needs remains a major challenge (1-15).

Non–adherence is a multifactorial issue due to physiologic, cognitive and functional decline, poor caregiver support, polypharmacy and complex regimens. For resilience we need a holistic and a tailored approach (1).

Weak adherence leads to a couple of unwanted results. The disease may worsen or become permanent. Chronic disease attacks may be more often and strong and infections may have higher complications. This may lead to more potent treatments having broader risks and a redeced quality of life. We overcome with increased costs and healthcares (2).

Polypharmacy and medication complexity is a big burden. Because of multiple disorders (hypertension, diabetes, thyroid disease, hyperlipidemia, cardiovascular disorders, cancer, cerebrovascular disorder) older adults take different drugs and with the addition of topical medications confusion is escalating. Skin medications are underestimated or feared because of the side effects. Due to their cognitive decline they may forget the strict dosing times and the difference between antifungals, steroids, emollients and antibacterials (3).

Functional decline because of artiritis, joınt stiffness, tremor and reduced mobility makes it laborous to apply the topical suggestions. They may not reach the distant parts for local treatments and moisturizing agents. Follow-up visits may be too bothersome due to impaired motility and cognitive deceleration (4).

Visional decline may impair the capacity to distinguish between medications, their expiry date and dosing meticulously (5).

Multiple topical products may be confusing and time-consuming. It is hard to apply a cream on a large surface or change a wound dressing regularly at those ages. You can see all of the problems addressed in the below table 1 (6).

Table 1 Problems in geriatric dermatologic treatments

Polypharmacy and medication load
Adverse drug reaction risk
Cognitive impairment
Functional decline and limited mobility
Visual and hearing decline
Socioeconomic factors
Poor communication
Health misconceptions and misbeliefs
Psychological factors

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DOI: 10.37609/akya.4051.c4832

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