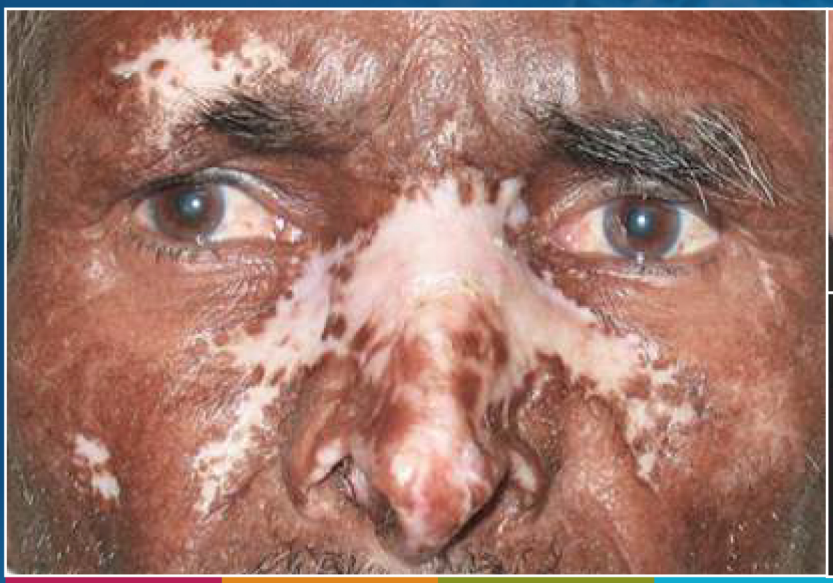
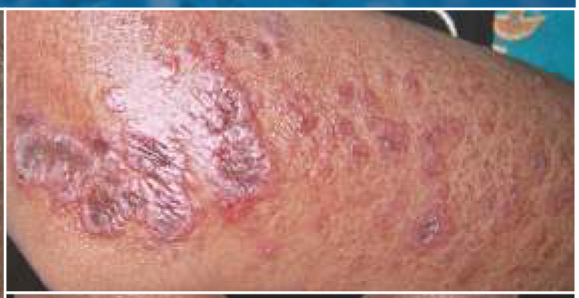
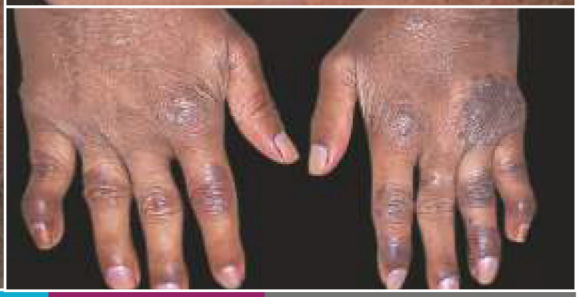
2nd Edn

Compendium of Dermatology *for* Examinations







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Contents

Chapter

1

Acne Rosacea

Pooja Arora Mrig

Introduction

Rosacea is a centrofacial skin disease characterized by flushing, erythema, telangiectasias and papulopustular lesions on the cheeks and nose. The clinical spectrum varies from mild involvement with erythema to severe disfiguring variants.

Epidemiology

- It is more common in fair skin types.
- It usually affects the middle aged and elderly with an age of onset between 30 and 50 years.
- Rosacea can rarely occur in children. Children more commonly present with rosacea-like conditions like perioral dermatitis.
- Gender predilection varies between different populations.

Pathogenesis

Pathogenesis of rosacea is multifactorial with interplay of several factors.

Genetics: Association found with polymorphisms nearby the BPTK316 as well as signals in the MHC class II molecules.

Environmental factors: Temperature changes, caffeine, hot and spicy foods, alcohol, sunlight, exercise, psychological stress, menstruation, demodex mites and certain medications. Role of *H. pylori* is not clear.

Toll-like receptors, cytokines and anti-microbial peptides: Toll-like receptor 2 (TLR2) and Toll-like receptor 4 (TLR4) found to be over-expressed in rosacea skin. AMPs are also increased.

Immune cells: T cells (especially Th1/Th17—polarized immune cells), macrophages, mast cells and neutrophils play an important role in pathogenesis. Reactive oxygen species (ROS) and other proteases are produced by inflammatory cells that lead to inflammation, angiogenesis, and telangiectasias. Recently, an involvement of B cells in the pathogenesis of rosacea was shown as well.

Blood vessels: Papillary dermal vessels are dilated resulted in erythema.

Nerves: Sensory nerve endings are activated to release vasoactive peptides that cause flushing and erythema.

Clinical Features and Differential Diagnosis

The most commonly used classification categorizes rosacea into various types based on clinical features. There is overlap in the clinical manifestations and one patient can have more than one subtype, though the various classic manifestations are depicted in **Fig. 1.1**. **Table 1.1** gives the classification with common differential diagnoses of the subtypes.

Table 1.1: Classification of rosacea with differential diagnosis

Subtype	Clinical features	Differential diagnosis
I. **Erythematotelangiectatic rosacea (ETTR)**	• Transient (flushing) or persistent erythema over centrofacial area **(Fig. 1.2)** • Edema • Telangiectasia • Skin sensitivity	• Other causes of flushing (physiological—menopause, anxiety, pathological—carcinoid tumors) • Actinic damage (telangiectatic photoaging) • Seborrheic dermatitis • Photoallergic or phototoxic reactions • Lupus erythematosus • Heliotrope rash of DM
II. **Papulopustular rosacea (PPR)**	• Persistent erythema (post-inflammatory, telangiectasia, vasodilation) • Erythematous papules/papulopustular that appear singly or in crops over centrofacial area • No residual scarring	• Papulopustular acne • Steroid-induced rosacea • Perioral dermatitis • Allergic dermatitis • Tinea incognito, candidiasis • Lupus miliaris disseminatus faciei • Cutaneous sarcoidosis • Gram-negative folliculitis • Eosinophilic folliculitis • Demodicosis
III. **Phymatous rosacea**	• Hyperplastic sebaceous glands along with fibrosis over nose and other facial regions seen as thickened nodular skin with prominent pores • Various types based on site involved: – Rhinophyma: Nose – Gnathophyma: Chin – Metophyma: Forehead – Otophyma: Ears – Blepharophyma: Eyelids	• Lupus pernio (sarcoidosis) • DLE • Cutaneous TB (lupus vulgaris) • Chilblain lupus • Neoplasms (angiosarcoma) • Eosinophilic granuloma
IV. **Ocular rosacea**	• Ocular changes may or may not be accompanied by cutaneous rosacea • Eye changes more common with subtypes I and II – Dry, gritty sensation, tearing, pruritus – Conjunctivitis – Keratitis – Blepharitis, scaling at eyelid margins, conical dandruff – Scleritis, episcleritis, iritis – Chalazia, hordeola	• Seborrheic dermatitis • Drug-induced ocular rosacea (eye drops) • Bacterial and viral conjunctivitis • Allergic conjunctivitis • Infectious keratitis

TREATMENT OF PEMPHIGUS

Principles of Treatment

The agents that are used are either targeted to the specific cells (T/B cells) or to the antibodies released. In essence, the use of steroids and ISA have a broad range of effects and hence have more side effects and thus the focus is on agents that are specific to the targets.

Published guidelines for pemphigus therapy mostly rely on expert consensus, given the paucity of randomized clinical trials with large sample sizes and rigorous randomization methods. The modalities of treatment of pemphigus foliaceous and vulgaris are similar. We shall briefly discuss some of the important therapeutic modalities in the following section.

The phases of therapy are given in **Table 4.10**, while an overview of the agents is given in **Table 4.11**; details of treatment follow in the text below.

Systemic CS (Boxes 4.5 and 4.6)

- Osteoporosis counselling should be provided if corticosteroid treatment is anticipated to last ≥3 months. Pneumocystis prophylaxis and tuberculosis screening should be considered for patients who will receive high doses of corticosteroids together with another immunosuppressive drug for >1 month.
- At the end of the consolidation phase of therapy, most clinicians begin to taper steroids. Approximately half of patients will relapse during steroid taper, whereas half will achieve complete remission off therapy after a mean treatment duration of 3 years.

Immunosuppressive Agents (ISA)

- Mycophenolate mofetil and azathioprine demonstrate approximately comparable safety and efficacy.
- Mycophenolate mofetil has shown faster and more durable treatment responses than placebo when added to prednisolone regimens.
- Azathioprine is generally preferred for patients with renal failure.

Disease Outcome Parameters

Some useful terms that help to stratify the disease response are given below.

- **Control of disease activity** (disease control)—time interval from baseline to the time at which new lesions cease to form and established lesions begin to heal.
- **End of the consolidation phase**—no new lesions × 2 weeks and the majority (approximately 80%) of established lesions have healed. Tapering of corticosteroid doses at this point.
- **Complete remission on therapy**—absence of new or established lesions while the patient is receiving minimal therapy (<10 mg/day of prednisone (or equivalent) and/or minimal adjuvant therapy × 2 months).

Table 4.10: Phases of treatment of pemphigus

Control	Intensive therapy is given until no new lesions appear for 2 weeks
Consolidation	Treatment is continued until the lesions completely clear
Maintenance	Lowest dose of the drug is given to prevent the appearance of any new lesions
Follow-up	During this period, the patients are advised for regular follow-up without any treatment

Table 4.11: Topical and systemic therapy

Topical	
• Good oral hygiene • Clobetasol propionate (mild pemphigus). Potent topical or intralesional steroids may reduce the requirement for oral steroids • Anticholinergic gel (pilocarpine) for oral erosions • Tacrolimus and cyclosporine • Intralesional triamcinolone acetonide (2.5–5 mg/ml) for intractable oral ulcers	
Systemic	
1. Steroids: The details of steroids and DCP are explained in **Boxes 4.5** and **4.6**	
2. Immunosuppressives:	
Cyclophosphamide	Cyclophosphamide is a potent anti-B cell agent. Dose: 1–3 mg/kg/day
Azathioprine	Dose: 2–3 mg/kg/day
Mycophenolate mofetil	An anti-metabolite that inhibits *de novo* pathway of purine synthesis in T and B cells. Dose: 1–3 g/day
Methotrexate	Dose: 10–50 mg/week
Cyclosporine	Dose: 2.5–5 mg/kg/day
3. Anti-inflammatory	
Dapsone	Pemphigus herpetiformis
Acitretin	With prednisolone in pemphigus vegetans
Gold	May have modest effect in pemphigus, though toxic effects limit its utility
Tetracycline, Nicotinamide	Tetracycline and/or nicotinamide in combination with prednisolone may be useful in mild disease.
4. Biologics and IVIG	
IVIG	Unclear mechanism, may have a dilutional effect on pathogenic autoantibodies plus anti-idiotypic effects. Dose: 2 g/kg split over 3–5 days
Rituximab	Chimeric monoclonal antibody against CD20. Dose: 375 mg/m^2 weekly for 4 weeks or two infusions of 1g, 2 weeks apart (*see* **Box 4.7** for details)
5. Desmoglein-specific immunoadsorption Extracorporeal photophoresis, plasmapheresis, immunoadsorption IVIG	
6. Desmoglein-specific B cell depletion Desmoglein 3 chimeric autoantibody receptor T cells (CAARTs) specifically bind to and kill anti-desmoglein 3 B cells, leading to disease remission in a pemphigus mouse model without immunosuppression	

- **Complete remission off therapy**—no new and/or established lesions off all systemic therapy × 2 months
- **Relapse/flare**—3 or more new lesions a month that do not heal spontaneously within 1 week, or the extension of established lesions, in a patient who has achieved disease control.
- **Failure of therapy**—failure to control disease activity (i.e. relapse/flare) with full therapeutic doses of systemic treatments.

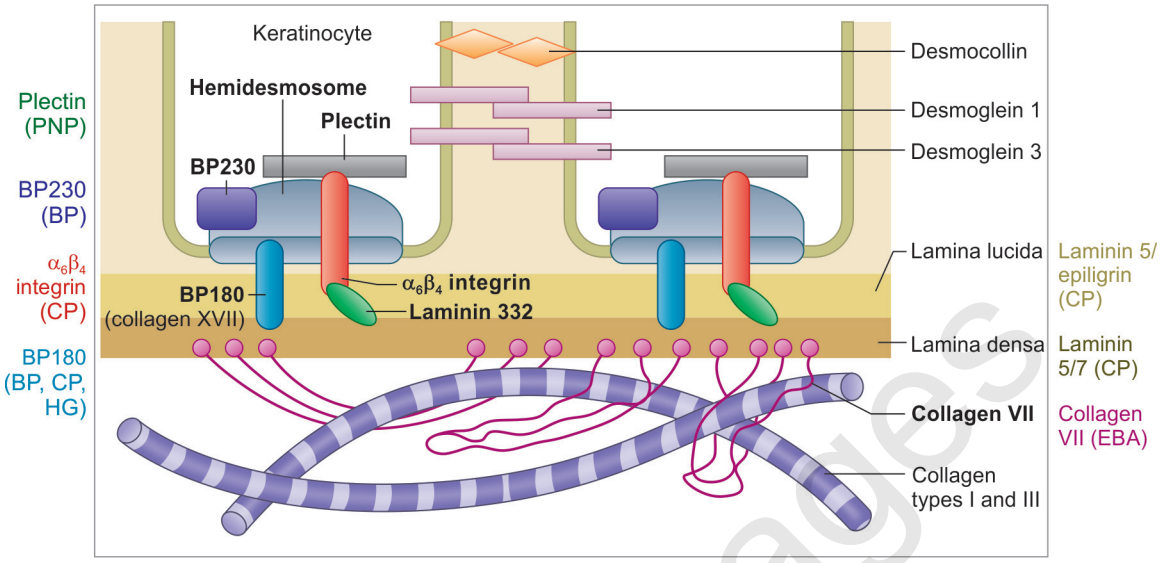


Fig. 4.10: A depiction of the hemidesmosome and BMZ with emphasis on the target antigens in the various structures of the BMZ. The major disorders are listed in brackets with the target antigen

Pathogenesis

- **Antigens:**
  BP180/type XVII collagen/BPAG2 (in 75–90%) and BP230/BPAG1 (in 50–70%)
  - Immunodominant region of BP180—**extracellular portion of the 16th non-collagenous domain (NC16A)** located directly adjacent to the cellular membrane.
    (explains why antibodies to both BP180 and BP230 can be seen in a significant portion of the population without blister formation as these are not against the critical NC16A region of BP180)
  - BP230 (BPAG1): 230 kDa cytoplasmic plaque protein belonging to plakin family; not the primary mediator of BP → antibodies are formed as secondary phenomenon (epitope spreading)
- **Antibodies: IgG4, IgG1**, also IgE and IgA
- Autoreactive T cells in BP patients produced a Th1/Th2 mixed cytokine profile. Th2 type cytokines are important in human BP. Th17 also plays a role.
- **IgE-anti-BP180 NC16A antibodies**—associated with severe disease, longer time-to-remission and need for more intensive therapy (Kamata A).
- **Complement activation and mast cell activation—crucial** for neutrophil and macrophage chemotaxis at the DEJ.
- The summary of pathogenesis of BP is depicted in **Fig. 4.11** (*see* **Box 4.9** for key).

Predisposing Factors

- Trauma, burns, skin grafting, radiotherapy
- UV radiation—sunlight, PUVA, PDT
- Influenza vaccination—doubtful role
- Drugs—**furosemide, spironolactone, phenothiazines,** other loop diuretics, penicillin, ampicillin, penicillamine, ciprofloxacin, potassium iodide, ACE inhibitors, antidiabetics

Chapter

9

Follicular Disorders

Ananta Khurana

- A group of disorders presenting with small papules localized around follicles and appendages.
- **True follicular disorders:** Present clinically with keratotic papules or papules with prominent spine and follicular plugging on histopathology **(Sardana K)**.
- Typically, follicular lesions do not have a tendency to coalesce.

Classification

An approach to the diagnosis of the follicular disorder is given in the **Flowchart 9.1**. These are conveniently divided into 3 broad types—keratotic papules, lichenoid papules and the Id eruptions. A regional classification is given in **Flowchart 9.2**. **Table 9.1** gives an etiological classification of the common follicular disorders.

The details of the common disorders seen are listed in **Table 9.2** and some are discussed in the text that follows.

KERATOSIS PILARIS (KP)

Etiopathogenesis: Not well understood but many factors, including histopathologic findings, the tendency to improve during adolescence, the association with filaggrin mutations and 18p monosomy, the effects of androgen and insulin dysregulation, and reduced prevalence in patients with acne vulgaris, support KP as a disorder of the sebaceous gland, which disrupts the permeability barrier of the SC and causes aberrant keratinization and hair abnormalities.

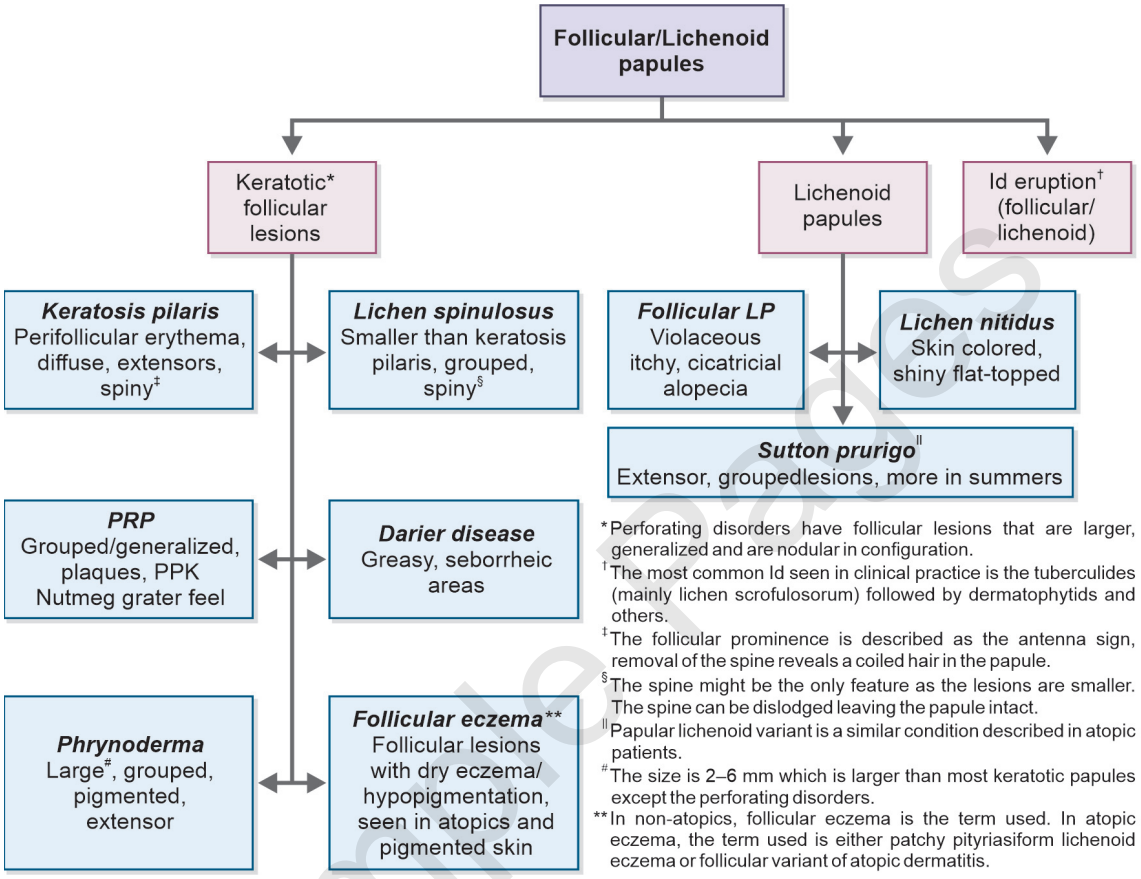
Onset: First two decades of life (peak at puberty)

Family history: Positive in 39%

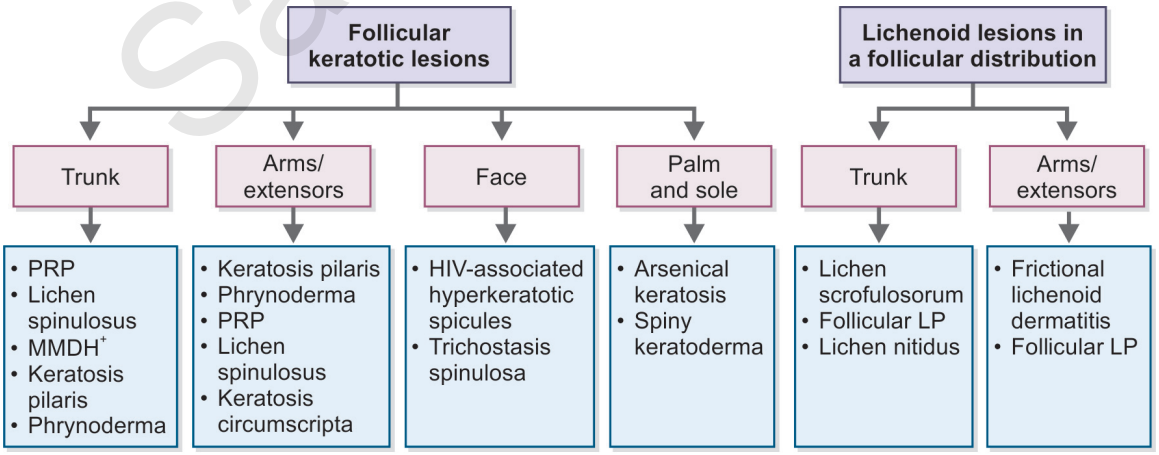
Clinical Presentation

- 'Chicken skin,' appearance.
- Keratotic papules in a folliculocentric distribution; **'antenna sign'** positive **(Fig. 9.1a)**.
- Distributed on the extensor surfaces of the proximal extremities.
- Variable amount of perifollicular erythema—present.
- Mild KP may have coiled or twisted vellus hairs, either single or in groups of 2–3, surrounded by peripilar casts.

Flowchart 9.1: An overview of the common follicular disorders based on the prominent morphology



Flowchart 9.2: A regional classification of follicular disorders



PRP= Pityriasis Rubra Pilaris; LP= Lichen Planus
MMDH+= Multiple Minute Digitate Hyperkeratoses (typically non-follicular)

DNA REPAIR DISORDERS

The human genome is made up of about 3 billion DNA base pairs containing an estimated 30,000 protein-encoding genes. This DNA is continually being damaged by a variety of endogenous sources (such as reactive oxygen species) and exogenous sources (such as ultraviolet and ionizing radiation). There are multiple elaborate mechanisms to avoid this damage and defects in these DNA repair pathways result in a number of disorders **(Table 10.17)**.

Table 10.17: DNA repair disorders

Nucleotide excision repair	• **Xeroderma pigmentosum** • Cockayne syndrome • Trichothiodystrophy
Recombination Q helicase	• **Rothmund-Thomson syndrome** • **Bloom syndrome** • **Werner's syndrome**
Double strand break repair	Ataxia telangiectasia
Interstrand cross-link repair	Fanconi anemia
Mismatch repair	Muir-Torre syndrome

Note: Those in bold are important for examinees.

XERODERMA PIGMENTOSUM (XP)

The term xeroderma pigmentosum, means "pigmented dry skin".
In Indian and Middle Eastern areas, the incidence is quoted at one per 10,000–30,000.

Defect and Clinical Correlates

- AR disorder due to mutations in XPA to XPG genes (as well as variant XPV gene)—each gene encodes a protein important in the nucleotide excision repair pathway:

  The defect is in the nucleotide excision repair (NER) pathways and is of two types: **(Fig. 10.43)**

  a. Global genome nucleotide excision repair (GG-NER) in which damage to DNA not undergoing transcription is repaired.
  b. Transcription-coupled nucleotide excision repair (TC-NER) in which damage in transcribed regions of DNA is rapidly repaired.
- GG-NER can globally repair lesions in the genome, whereas TC-NER will only repair lesions on actively transcribed genes. The **subtypes** (7 complementation groups) of XP (XPA to XPG) correspond to the affected genes **either of nucleotide excision repair (NER) (XPA-XPG) or translesion synthesis (XPV)**.

  1. Steps unique to **GG-NER involve XPC and XPE**. Patients with defects in XPC and XPE show evidence of **freckling** but generally do **not** have an abnormal **sunburn reaction**. **However, they have highest increased risk of skin cancer**, which is thought to be at least partly attributable to the fact they do not have the adverse reaction to sun-light that would lead them to avoid sun exposure.

     Patients in the XPC complementation group have also recently been observed to have high sensitivity to ocular damage.

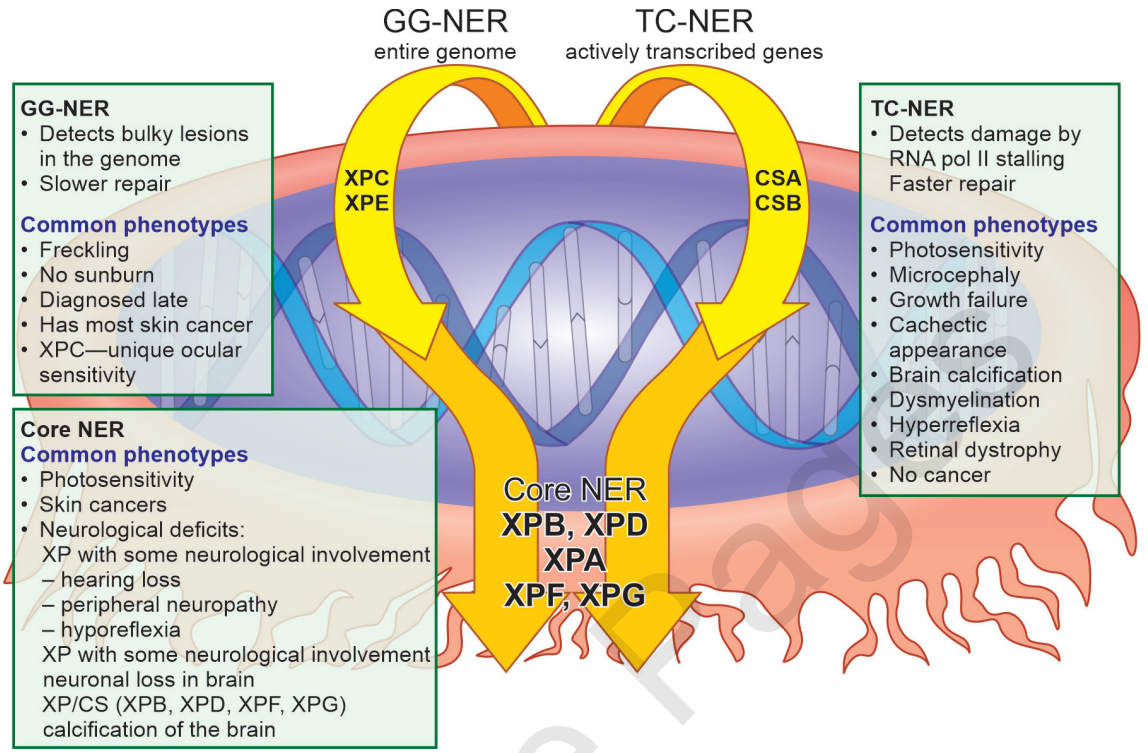


Fig. 10.43: Correlation of phenotypes with molecular deficits in xeroderma pigmentosum (XP). The two types of nucleotide excision repair (NER), global genome NER (GG-NER) and transcription-coupled NER (TC-NER), are shown. After initial recognition of the DNA damage, GG-NER and TC-NER both utilize a common pathway with core NER proteins for excision and repair

2. Steps unique to **TC-NER involve two genes** (CSA, CSB) involved in Cockayne syndrome (CS).
3. The core **NER proteins**, are utilized by both GG-NER and TC-NER, include **XPA, XPB, XPD, XPF and XPG**.
   Clinical features are of both GG-NER and TC-NER phenotypes, both skin cancer and neurological abnormalities.
4. XPV group have mutations in polymerase: Similarly to patients with XP who have mutations in proteins involved in the initial steps of GG-NER (XPC, XPE), patients in the XPV group do not present with abnormal sun-burn reactions and also show high susceptibility to developing skin cancer, albeit later in life.
5. A summary is given below:
   - Most common subtypes in the United States are XPA and XPC; XPA is most common subtype in Japan.
   - Broad range of neurological involvement in XP, including XP with some neurological features, XP with severe neurological features (which can be associated with mutations in XPA), and those with XP/CS complex common in Japan.
   - De Sanctis-Cacchione syndrome: Rare XP phenotype with severe neurologic deficits (severe mental retardation, deafness, at axia and paralysis). This term is no longer in general use as it is now appreciated that XP can be associated with neurological problems of widely varying severity.

CORYNEBACTERIAL CUTANEOUS INFECTIONS

ERYTHRASMA

Cause

C. minutissimum.

Epidemiology

- More in diabetics
- Although clinically most common on groin and axillae, Wood's lamp evidence suggests maximum in toe clefts.

Predisposing Factors

- Warm humid climate
- Diabetes mellitus

Clinical Features (Fig. 14.6a)

- Sites—groin, axillae, submammary, intergluteal
- Sharply marginated irregular red smooth patches → brown scaly later

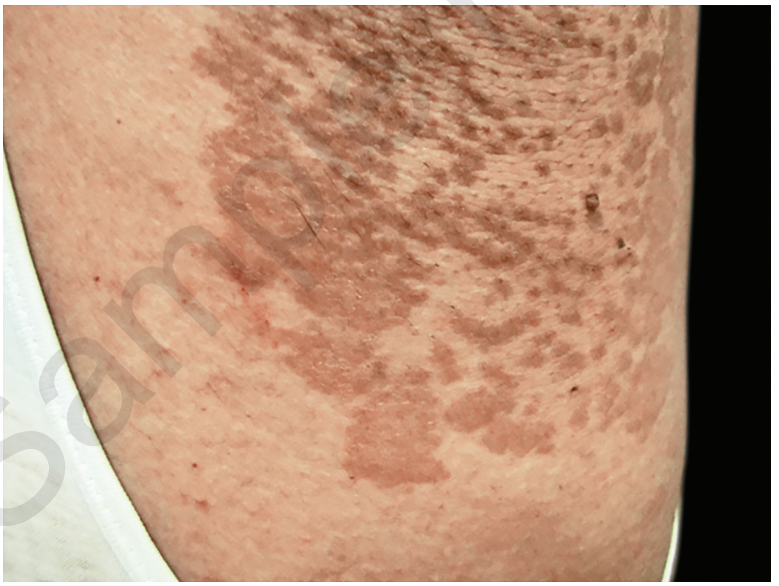


Fig. 14.6a: Erythematous 'relatively' non-itchy lesion of erythrasma

Diagnosis

- **Bedside tests**
  - Wood's lamp—*coral-red/pink fluorescence* (coproporphyrin III by coryneforms).

Differential Diagnosis (Box 14.1b)

- Pityriasis versicolor—occurs on upper trunk, smaller lesions, not erythematous.
- Tinea cruris—inflammations +, active raised border, satellite lesions absent.

Diagnosis

- **Bedside tests**
  - KOH mount
  - Gram stain
  - Culture—in blood agar

Differential Diagnosis

- Pediculosis pubis—matting of pubic hair, no concretions, lice can be visualized by dermoscopy.
- Piedra—scalp and beard more common, KOH mount shows hyphae.

Treatment (Fig 14.7b)

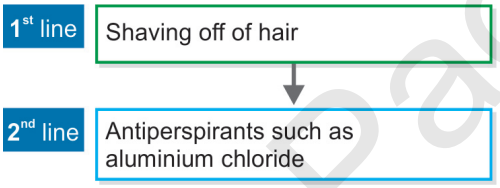


Fig. 14.7b: Treatment of trichomycosis axillaris

PITTED KERATOLYSIS

Cause

Corynebacterium spp, *Actinomyces keratolytica*, *Dermatophilus congolensis*, *Kytococcus sedentarius*, etc.

Predisposing Factors

- Warm humid climate
- Hyperhidrosis

Clinical Features

- Sites on soles—pressure-bearing/friction areas **(Fig. 14.8a)**
- Conspicuous, discrete, shallow, circular, punched out superficial erosions, coalescing at places to form irregular erosions.

Diagnosis

- **Bedside tests**
  - Gram stained smears
  - Culture on brain heart infusion agar

Chapter

16

Lichen Planus and Lichenoid Disorders

Surabhi Sinha, Kabir Sardana, Snigdha Saxena

LICHEN PLANUS (LP)

Epidemiology

- Cutaneous LP occurs in 0.2–1% adult population and mucosal LP in 1–4%
- Onset between fifth and sixth decade.
- Classically does not occur in infants and elderly.

Genetic Factors

Genetic susceptibility to idiopathic LP is known. HLA-A3 and HLA-A5, TNF-α gene polymorphism have been reported.

Environmental Factors

- **Postulated associated microorganisms**: Hepatitis C virus, hepatitis B virus, human herpes virus-6, human herpes virus-7, varicella zoster, hepatitis B vaccine (usually after second dose, associated with oral LP, and bullous LP in children). Hepatitis C: Strongly implicated in subset of oral (ulcerative/erosive) LP.
- **Drugs**—anti-microbials, anti-hypertensives, anti-malarials, anti-depressants, anti-convulsants, diuretics, metals, NSAIDs, imatinib, IVIg, etanercept and adalimumab.
- **Dental amalgam (mercury)**
  - Associated with oral LP
  - 95%/improve with removal of sensitizing metal
  - Even with negative patch test, 75% clear when metal is removed
- Betel nut
- Radiotherapy
- Anxiety, stress and depression (might be the cause or may result from LP).

Pathophysiology

T cell-mediated autoimmune disease targeting the basal keratinocytes, triggered by a variety of situations, including viruses, drugs and contact allergens.

The various steps of pathogenesis are elucidated in **Box 16.1** and are shown in **Fig. 16.1**. The varied theories encompass three major stages—antigen recognition, lymphocyte activation, and keratinocyte apoptosis and have firm data, but the most relevant to clinicians-resolution, is a new and emerging topic that awaits more data.

Box 16.1: Overview of pathogenesis of LP

- Earliest change—increased numbers of LC.
- CD8 cells predominate in epidermis and CD4 in dermis.
  1. Initiation phase: Damage to keratinocytes results in stimulation of pDCs and release of IFN-α.
  2. Stimulated mDC present CD4-Th cells with the antigen (unknown as yet).
  3. LCs and other APCs in epithelium present Ag (currently unknown) via MHC-II to CD4 cells, while basal cells present Ag via MHC I to CD8 cells → activate CD8 cells.
- CD4 cells secrete IL-2 and IFN-γ → activate CD8 cells.
- Activated CD8+ T cells induce keratinocyte apoptosis through 1 of 3 mechanisms—secretion of tumor necrosis factor (TNF)-α, secretion of granzyme B, or Fas-Fas ligand interactions.
- Activated CD8+ T cells produce chemokines—IL-2, 4, 6, TNF-α, IFN-γ—that attract additional inflammatory cells, thereby promoting continued inflammation.
- Chemokines released by CD8 cells interact with keratinocytes and cause apoptosis.
- Mast cells sustain the inflammation and secrete MMP/Chymase/Tryptase → basement membrane damage.
- **Cytokines:** IFN-γ, IL-6, granulocyte-macrophage colony-stimulating factor (GM-CSF), and tumor necrosis factor alpha (TNF-α).
- **Major kill signals:** TNF-α, granzyme, and perforin. Fas and Fas ligand (Fas-L) are expressed on both keratinocytes and lymphocytes and causes apoptosis as well as disease resolution.

LC: Langerhans cells; CTL: Cytotoxic T lymphocyte; MDC: Myeloid dentritic cells; pDC: Plasmacytoid dendritic cells

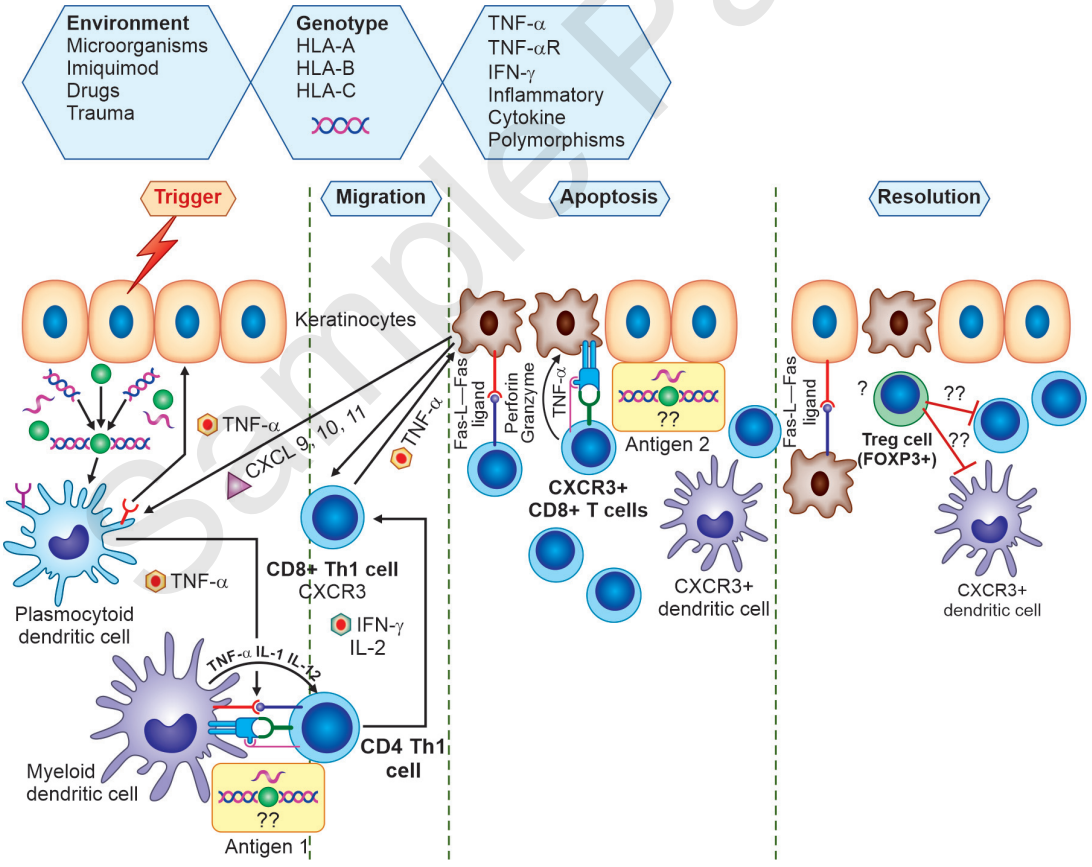


Fig. 16.1: Pathogenesis of LP: Numerous trigger factors have been implicated. The initiation phase leads to stimulation of plasmacytoid dendritic cells (pDC) with release of IFN-α. This leads to stimulation of CD4– T cells which in turn stimulate CD8– T cells which damage keratinocytes and can induce apoptosis

Chapter

28

Reactive Arthritis (Reiter Disease)

Surabhi Sinha, Bhawuk Dhir

Reactive arthritis (ReA), previously known as Reiter disease, is a part of the spectrum of the spondyloarthropathies (usually RA factor seronegative).

It refers to an infection-induced systemic illness, characterized by a triad of urethritis, conjunctivitis/iritis, and arthritis (sterile synovitis) ("*can't see, can't pee, can't climb a tree*") occurring in a genetically predisposed individual, secondary to a bacterial infection localized in a distant organ/system, usually in the genitourinary (GU) or/and gastrointestinal (GI) tract.

Definitions

Reactive arthritis: Aseptic inflammatory arthritis, triggered by infection at a distant site, in genetically susceptible people.

Reiter syndrome (classic definition): A triad of urethritis, conjunctivitis, and arthritis secondary to an infectious dysentery.

Reiter syndrome (ACR definition): Episode of peripheral arthritis of more than one month's duration occurring in association with urethritis or cervicitis.

Uroarthritis: Reactive arthritis secondary to a urinary tract infection.

Sexually acquired reactive arthritis (SARA): Reactive arthritis associated with a recent sexually transmitted infection.

Epidemiology

ReA usually manifests itself as arthritis 2–4 weeks following GU or GI infections, sometimes up to 6 months, often with HLA-B27 positivity.

ReA is more frequent in males under 40 years old.

Etiopathogenesis

The relationship between bacteria and genetics is well-illustrated in ReA.

The exact role of action of **HLA-B27** in spondyloarthropathies is not known; 30 to 40% of patients with ReA are positive for this antigen; one theory postulates that HLA-B27 presents arthritogenic bacterial peptides to T cells, stimulating an autoimmune response (molecular

mimicry). Another theory is that HLA-B27 cells may act as an autoantigen that is targeted by the immune system. There also appears to be molecular mimicry between the infective organisms and a region of the HLA-B27α-I helix. The risk of developing ReA is 50 times higher in a HLA-B27 positive individual.

Toll-like receptors: TLR-4 can recognize lipopolysaccharides and could have a role in ReA. TLR-2 has also been associated with ReA.

Pathogens

A long list of bacteria has been described as triggers of ReA that can reach the joints through intestinal or genitourinary infections; these bacteria may reach the joints as a complete form or as fragments **(Table 28.1)**. Most are intracellular organisms. *Chlamydia trachomatis* is proposed to be the most common cause of ReA (genitourinary transmission); *Ureaplasma urealyticum* and occasionally *Neisseria gonorrohoeae* have been described.

Clinical Features

Classified as acute (<6 months) and chronic (>6 months). Further subdivided into articular and extra-articular **(Table 28.2)**.

Diagnosis

The consensus diagnostic criteria as per Third International Workshop on Reactive Arthritis, 1995 are given in **Box 28.1**.

Differential Diagnosis

The commonest differential diagnosis is psoriatic arthritis (PsA). Though there are many similarities between the various types of SpA and even RA, **Table 28.3** lists some differentiating features and **Fig. 28.2** shows a diagnostic algorithm of reactive arthritis and spondyloarthropathy.

Table 28.1: Arthritogenic agents associated with the development of reactive arthritis

Enteric infections	Urogenital infections	Respiratory infections	Others
Probable	***Probable***	***Possible***	• HIV
• *Shigella flexneri, S. dysenteriae, S. sonnei*	• ***Chlamydia trachomatis****	• *Chlamydia pneumoniae*	• B-19 parvovirus
• *Yersinia enterocolitica, Y. pseudotuberculosis*	***Possible***	• Group A beta-hemolytic *Streptococcus*	• *Borrelia burgdorferi*
• *Campylobacter jejuni, C. coli*	• *Ureaplasma urealyticum*		• *Brucella abortus*
• *Salmonella enteritidis, S. typhimurium*	• *Mycoplasma genitalium*		• Bacillus Calmette-Guerin
Possible	• *Neisseria gonorrhoeae*		• Chikungunya virus
• *Clostridium difficile*			
• *Escherichia coli*			
• *Bacillus cereus*			
• *Cryptosporidium, Giardia lamblia*			
• *Helicobacter pylori, H. cinaeli*			
• *Strongyloides* spp.			
• *Tropheryma whipplei*			

*Most commonly implicated urogenital pathogen causing ReA

Chapter

32

Xanthomas and Hyperlipoproteinemia

Kabir Sardana, Surabhi Sinha, Sweta Singh

Hyperlipoproteinemias are clinically characterized by subcutaneous lipid deposits (xanthomas).

Overview of Lipoprotein Transport

- Lipoprotein transport plasma lipids to peripheral cells. **Figure 32.1** depicts the transport and metabolism of triglycerides (TG).

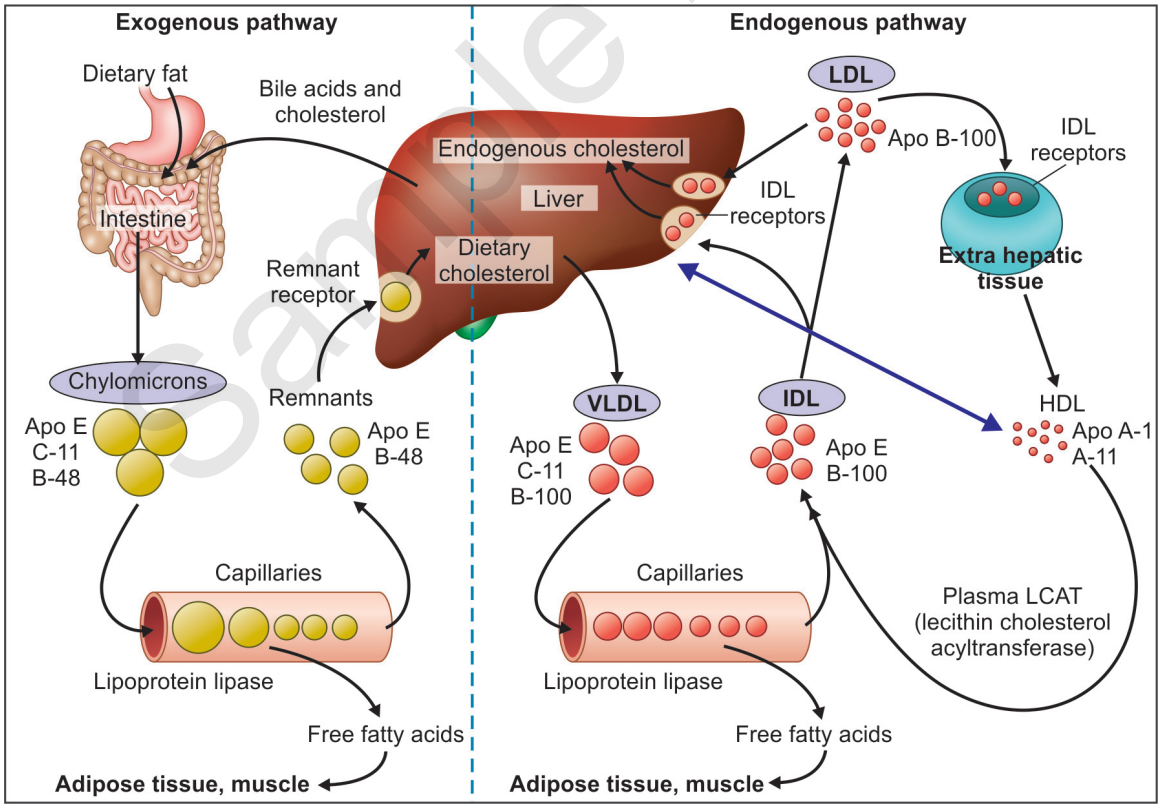


Fig. 32.1: Overview of lipoprotein metabolism and transport

- Types of lipoproteins:
  i. **Chylomicrons:** Mainly *exogenous production*
  Central core of mainly triglycerides; outer shell contains various apoproteins (B-48, E, A-I, A-II, and C-II).
  Becomes *chylomicron remnant* after most of the triglyceride content is hydrolyzed.
  ii. **VLDL:** Mainly *endogenous production* in liver.
  Central core of mainly triglycerides; outer shell contains B-100, E and C-II. C-II needed for lipoprotein lipase activation.
  iii. **IDL:** Remnant of VLDL after hydrolysis of most of the triglycerides by lipoprotein lipase
  iv. **LDL:** Product of further triglyceride hydrolysis of IDL (now mainly cholesterol ester core and B-100 on surface).
  Uptake into *hepatocytes* by apo B-100/E.
  v. **HDL:** *Removes cholesterol* from tissues. Free cholesterol esterified by lecithin: Cholesterol acyltransferase. Requires apoprotein A-I on HDL **(Fig. 32.1)**.

Clinical Types, Pathogenesis and Treatment of Hyperlipoproteinemias

An overview of the **hyperlipoproteinemias** is listed in **Table 32.1**.

Clinical Features

The clinical features can be localized to the skin or systemic and are listed in **Table 32.1**. As xanthomas are an obvious clinical marker, a detailed overview and the possible disorders are listed in **Table 32.2** and depicted in **Figs 32.2** and **32.3**.

Investigations

I—**plasma chylomicrons, triglycerides markedly** ↑; cholesterol normal; very low-density lipoprotein (VLDL), high-density lipoprotein (HDL), low-density lipoprotein (LDL) normal or decreased; enzyme assay for lipoprotein lipase/apo C-II activity; **creamy top layer** on standing at 4°C for 18 hours.
II—plasma **LDL, cholesterol** markedly ↑; LDL receptor assay; **turbid plasma**.
III—plasma **cholesterol, triglycerides** ↑; presence of beta-VLDL on lipoprotein electrophoresis; apoE phenotyping; **turbid plasma**.
IV—plasma **VLDL, triglycerides** markedly ↑; turbid plasma.
V—plasma **chylomicrons, triglycerides, VLDL** markedly ↑; cholesterol increased; **creamy top layer**.

Treatment

1. Close routine care by primary physician-screen children with family history of early infarcts, hyperlipoproteinemia
2. Nutritional management:
   I, V—restriction of fat intake/medium-chain triglyceride diet
   II—low-fat, low-cholesterol diet with reduction of saturated fats, increase in polyunsaturated and monounsaturated fats
   III—low-calorie/cholesterol/saturated-fat diet
   IV—low-calorie, low-carbohydrate diet
3. Plasmapheresis, liver transplantation (II)
4. Medical therapy: Lipid lowering agents including HMG-CoA reductase inhibitors, nicotinic acid, gemfibrozil, cholestyramine (II, III, IV, V).
5. Treatment of diabetes, hypothyroidism, obesity (III, IV, V).

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Editors

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