Viva questions from the IJDVL

TARGETED PHOTOTHERAPY

What is targeted phototherapy?

Targeted phototherapy, focused phototherapy or microphototherapy involves the application of light energy directly focused on a targeted lesion through special delivery mechanisms such as fiber optic cables. Targeted phototherapy includes:

- Excimer laser
- Intense pulsed light
- Light-based targeted phototherapy
- Photodynamic therapy
- Low level laser and light emitting diode therapy.

What is the mechanism of action of targeted phototherapy devices?

Most targeted phototherapy devices (laser or non-laser type) emit radiation in the ultraviolet B range with peak emission in the narrow band wavelength (around 308–311 nm) while some nonlaser systems emit ultraviolet A radiation also. The 308 nm xenon chloride laser uses noble gas with halogen as the lasing material. Ultraviolet B radiation induces alteration of cytokine production, local immunosuppression, stimulation of melanocyte stimulating hormone, increased melanocyte proliferation and melanogenesis. In targeted phototherapy, all these effects are induced in a more aggressive fashion because of delivery of super-erythemogenic doses of radiation.

What are the indications of targeted phototherapy?

Common indications of targeted phototherapy include:

- Stable vitiligo – localized vitiligo that is resistant to the other modalities of treatment
- Psoriasis – localized resistant lesions on the hands and knees, scalp psoriasis
- Other indications – oral lichen planus, atopic dermatitis, mycosis fungoides, lymphomatoid papulosis, hypopigmented striae and scars.

What are the differences between targeted phototherapy and conventional phototherapy?

The salient differences between conventional and targeted phototherapy have been outlined in Table 1.

Table 1: Salient differences between conventional and targeted phototherapy

Conventional phototherapy	Targeted phototherapy
Exposure of uninvolved areas	Exposure of involved area and sparing of the uninvolved areas
Slow delivery, lengthy treatment sessions	Quick delivery of energy and shortened duration of treatment
Multiple and frequent visits to the clinic	There is delivery of higher (super erythemogenic) doses of energy because uninvolved areas are not exposed. Higher doses of energy can be delivered selectively to the lesions thereby increasing efficacy and achieving faster response. Hence, it shortens duration of treatment leading to less frequent visits to the clinic and thereby lessens the inconvenience to the patient
Difficulty in treating certain areas such as genitalia, oral mucosa and ear	The maneuverable hand piece allows treatment of difficult areas such as scalp, nose, genitals, oral mucosa and ear
Difficulty in treating children who may be intimidated by the large machines	Easy administration as machine is handheld
Large office space required to house bulky machines	Target phototherapy machines occupy much less space
Less expensive	More expensive
Can be used to treat extensive areas	Not adequate to treat extensive areas in view of cost of treatment and time involved in the treatment. Hence, not recommended for use if lesions occur on more than 10% of the body surface area
Claustrophobia can occur in the phototherapy booth	No such problem encountered
Lesser risk of blistering and burning of the treated area	Possible risk of burning and blistering crusting of the treated area

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TOXIC EPIDERMAL NECROLYSIS

What are the common drugs causing Steven–Johnson syndrome/toxic epidermal necrolysis?

Steven–Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN) can be caused by any drug, but the high-risk drugs are carbamazepine, phenytoin, allopurinol, lamotrigine, oxicam and other nonsteroidal anti-inflammatory drugs, sulfonamide antibiotics and nevirapine.

What are the infections that can cause toxic epidermal necrolysis?

Mycoplasma and cytomegalovirus infections can cause toxic epidermal necrolysis.

Briefly outline the management of toxic epidermal necrolysis

Management of toxic epidermal necrolysis involves basic supportive treatment along with the use of specific drugs. These have been outlined in Box 1 and Table 2.

What are signs of sepsis in cases of toxic epidermal necrolysis?

- General deterioration of the patient
- Hypothermia
- Fever/shivering
- Diminishing level of consciousness
- Falling urine output
- Deterioration of respiration
- Loss of diabetic control
- Failure of gastric emptying
- Sudden change in the condition.

What is SCORTEN (severity-of-illness score for toxic epidermal necrolysis)?

"SCORTEN" (severity-of-illness score for toxic epidermal necrolysis) is a validated mathematical tool for prognostication of Steven–Johnson syndrome/toxic epidermal necrolysis patients. It should be computed within 24 h after admission and again on the third day. The index identifies the following seven independent risk factors for death.

Box 1: Basic supportive treatment in TEN

Instant cessation of the offending drug

Admit the patient in a burns unit/ICU or general dermatology ward/high dependency unit with strict infection control and trained nurses

Evaluate airway, breathing, circulation, urine output and percentage of body surface area involved. Catheterize the patient if required

Environmental temperature: 30-32°C

Use of air bed/water bed. Frequent change in position

Barrier nursing

Empirical antibiotic

- Gram-positive cover – Amoxicillin clavulanic acid/tetracyclines/vancomycin,/clindamycin/teicoplanin/linezolid
- Gram-negative cover – Amikacin/piperacillin + tazobactam, cefoperazone + sulbactum/imipenem
- Anaerobic cover – Metronidazole/tinidazole

Investigations – Complete blood count, urine routine and microscopy, liver function tests, renal function tests, serum electrolytes, HIV testing, blood culture, catheter tip culture (cultures are to be done at admission and repeated every 48 h)

Fluid and electrolyte balance to be maintained through large-bore intravenous lines. Peripheral lines are preferable to central lines

- Fluid requirement is 2/3 to 3/4 of that for burns patients
- Fluid requirement = 4 ml/kg/body weight × percentage of BSA involved
- Half the calculated amount to be administered in the first 8 h and the other half over the next 16 h
- Maintain urine output between 1000 and 1500 ml/day

Feeding: enteric route is preferred. If not possible, nasogastric tube feeding/total parenteral nutrition can be given

- Caloric requirements: 30-35 kcals/kg/day. Protein requirements: 1.5 g/kg/day

Topical antiseptics: potassium permanganate (1:10,000), gentian violet, silver nitrate, chlorhexidine (silver sulfadiazine should be avoided)

Dressings: paraffin/petrolatum gauze/chlorhexidine impregnated dressing/collagen dressings

Oral care: normal saline squishes/antiseptic, anesthetic mouth washes. Saline lip compresses with petroleum jelly

Ophthalmic care: lubricant + antibiotic eye drops/ointments with or without corticosteroids (every 2 h)

Respiratory care: Normal saline aerosols, bronchial aspiration, postural drainage, moisturization with saline and removal of nasal crusts

Antacids/analgesics (opioid analgesics such as tramadol)/anxiolytics/antipyretics

Anticoagulation with heparin and early mobilization

Psychological care: emotional support and continual dialogue with family

TEN: Toxic epidermal necrolysis, ICU: Intensive Care Unit, HIV: Human immunodeficiency virus, BSA: Body surface area, NS: Normal saline

Table 2: Drugs used in the management of TEN

Drug	Mechanism of action in TEN	Dose/duration	Side effects
Corticosteroids	Suppression of TNF-α, IFN-γ, IL-6, IL-10, inhibition of IFN-γ induced apoptosis and inhibition of Fas-mediated keratinocyte apoptosis	High doses in a short period with rapid tapering	Increased morbidity, complications such as sepsis, leukopenia, thromboembolism, gastrointestinal ulcerations, prolonged recovery, worse prognosis and reduced survival
Cyclosporine	Inhibits the principal cellular populations involved in pathogenesis of TEN, i.e., activated T cells, macrophages and keratinocytes Interferes with metabolism of TNF-α and possesses anti-apoptotic properties	3-5 mg/kg/day Oral or intravenously for up to 2 weeks followed by weaning on another 2 weeks	Hypertension, renal toxicity. Though this is not much of a problem with the short duration of treatment
Intravenous immunoglobulin	Widespread apoptosis in SJS – TEN is partially mediated by binding Fas –L with CD95 death receptors and TNF-α R1 receptors present in keratinocytes. Intravenous immunoglobulin possess anti-Fas activity in a high concentration, Fas blocking antibodies inhibits keratinocytes apoptosis by blocking binding of Fas –L to Fas receptors. It also has anti-infectious properties and corrects protein and fluid loss	Considered if patient is seen within 48-72 h of the onset of Bullae. If clinical progression beyond 72 h may still be useful. Total dose: 2 g/kg, 0.4 g/kg/day for 5 days	Rule out thromboembolism, hemolysis, vasomotor symptoms, anaphylactic reactions
Other drugs that have been used include cyclophosphamide, pentoxifylline, N-acetyl cysteine, thalidomide, tacrolimus			

SJS: Stevens–Johnson syndrome, TEN: Toxic epidermal necrolysis, TNF-α: Tumor necrosis factor α, IFN-γ: Interferon γ, IL: Interleukin

- Age above 40 years
- Presence of malignancy
- Tachycardia (heart rate above 120 beats/min)
- Initial percentage of epidermal detachment above 10%
- Blood urea nitrogen above 28 mg/dl
- Serum glucose above 252 mg/dl
- Bicarbonate level <20 mmol/L.

Each parameter is given a score of one and the total score is calculated by summing up the number of abnormal parameters. Table 3 shows the mortality rate according to SCORTEN score. The most common causes of death are sepsis, pulmonary failure and multiple organ failure.

Table 3: Mortality rates according to SCORTEN level

SCORTEN	Mortality rate (%)
1	3.2
2	12.1
3	35.3
4	58.3

SCORTEN: Severity-of-illness score for toxic epidermal Necrolysis

ICTHYOSIS BULLOSA OF SIEMENS

What is mauserung phenomenon?

A distinctive feature of ichthyosis bullosa of Siemens which is not present in other forms of ichthyosis is called mauserung phenomenon (mauserung in German means "moulting" and was first described by Dr. H W Siemens). These are small patches of bare apparently normal skin (due to regeneration of the epidermis) in the middle of areas of hyperkeratosis. It is frequently seen at hyperkeratotic flexures and acral sites, especially on the dorsa of the hands and feet.

Enumerate the differences between bullous ichthyosiform erythroderma and ichthyosis bullosa of Siemens

The salient differences have been outlined in Table 4.

What is keratinopathic ichthyosis?

The term epidermolytic hyperkeratosis describes the characteristic light microscopic observation of intracellular vacuolization, clumping of tonofilaments and formation of small intraepidermal blisters and is commonly seen in ichthyosis due to keratin mutations. Therefore, the term epidermolytic hyperkeratosis is used (by some) as synonymous with bullous ichthyosis, ichthyosis exfoliativa, bullous congenital ichthyosiform erythroderma (of Brocq), ichthyosis bullosa of Siemens. To simplify the nomenclature, Vinzenz *et al.* proposed the umbrella term of "keratinopathic ichthyosis."

OCHRONOSIS

Enumerate the various types of ochronosis

Exogenous ochronosis is commonly due to topical hydroquinone use; other causative agents include phenol, resorcinol, mercury, picric acid, benzene and systemic antimalarial-like quinine. These agents inhibit homogentisic acid oxidase in the skin resulting

Table 4: Differences between BIE and ichthyosis bullosa of Siemens

BIE	Ichthysosis bullosa of Siemens/ superficial epidermolytic ichthyosis
Mutation in gene K1, K10	Mutation in Keratin 2 e
Greater severity	Milder variant of BIE
Erythroderma present at birth	Erythroderma absent
Presents within few hours of life	Presents within few days or weeks after birth
Mauserung absent	Mauserung present
Keratotic plaques are seen onr bony prominences. Eroded base when keratotic plaques are dislodged	Localization of dark gray hyperkeratosis to the flexural sites
Palmoplantar keratoderma is marked	Palmoplantar keratoderma is absent
Emollients do not help much. Retinoids and keratolytics are useful	Emollients are the mainstay of treatment. Low dose retinoid can be used in some patients

BIE: Bullous ichthyosiform erythroderma

in local accumulation of homogentisic acid which then polymerizes into the ochronotic pigment.

Endogenous ochronosis or alkaptonuria is an inborn error of metabolism. It is an autosomal recessive disease caused by a deficiency of homogentisic acid oxidase resulting in the accumulation of homogentisic acid in various tissues such as cartilage, tendons, ligaments or sclerae and is associated with dark urine.

Idiopathic ochronosis is characterized by the absence of use of any drug, features of alkaptonuria are absent and laboratory tests of blood and urine are negative.

Describe the histopathological features of ochronosis

Classical ochronosis shows the characteristic ochre or yellow-brown pigment. The pigment is present within collagen bundles which tend to fracture transversely resulting in pointed ends. Hence, these have been described as banana-shaped fibers or comma-shaped structures. Fine granules of ochronotic pigment may also be seen intracellularly in the endothelium, macrophages and secretory cells of sweat glands, as well as extracellularly, particularly in basement membranes. Collagen degeneration or granuloma formation may be occasionally seen. The ochronotic pigment does not stain with silver nitrate but shows blackish coloration with methylene blue or cresyl violet staining.

CRUSTED SCABIES

What is crusted scabies?

Crusted scabies is a distinct clinical subtype of scabies occurring due to hyperinfestation by *Sarcoptes scabiei* with the mites numbering in millions. It was first described in Norway in 1848. It develops due to a Th1/Th2 imbalance, with a cytotoxic T-cell type 2 response in the skin, high levels of antibody in the blood and uncontrolled growth of the parasite.

Enumerate the underlying conditions associated with crusted scabies

Crusted scabies is associated with immunosuppressed states due to topical or systemic glucocorticoid therapy, human immunodeficiency virus infection, human T lymphotropic virus 1 infection, T-cell lymphoma and leukemia or following organ transplant. It has also been noted in physically or mentally handicapped, senile bedridden individuals or patients with neurological diseases such as Parkinson's disease, Down's syndrome and patients with poor sensory perception (due to leprosy, spinal injury, syringomyelia, etc.). It has also been associated with previously treated leprosy, substance abuse, systemic lupus erythematosus, pulmonary tuberculosis, diabetes mellitus and hepatitis B. It has also been documented as a manifestation of immune reconstitution inflammatory syndrome in human immunodeficiency virus infection.

Enumerate the differential diagnosis of crusted scabies

Clinical presentation of crusted scabies includes hyperkeratotic crusted lesions on the hands and feet with deformed nails, generalized erythematous scaly rash and lesions on the scalp. Crusted scabies can mimic psoriasis, hyperkeratotic eczema, contact dermatitis, cutaneous lymphoma, Darier's disease or lichenoid dermatosis.

Describe the dermatoscopic and reflectance mode confocal microscopic findings in scabies

Both these techniques are non-invasive methods for the diagnosis of scabies. The mite, eggs and fecal pellets can be demonstrated.

The "jet with contrail" appearance of the mite in its burrow on dermatoscopy is characteristic.

Reflectance-mode confocal microscopy is a novel non-invasive imaging technique for skin structures

and lesions at a resolution comparable to that of conventional histology. With this technique, the burrows can be detected as multiple tortuous large segments in the stratum corneum and at the end of the burrows, mites can be identified. Roundish, refractile, oval particles corresponding to eggs and mite feces can also be visualized. Parakeratosis is demonstrated by the presence of highly refractile round to polygonal structures.

CUTIS VERTICIS GYRATA

Describe the clinical features of cutis verticis gyrate

Cutis verticis gyrata is a rare condition wherein the skin on the scalp is thickened and thrown into folds forming deep furrows and convoluted ridges, resembling the gyri and sulci of the cerebral cortex.

Classify the types of cutis verticis gyrata

Cutis verticis gyrata is classified into primary and secondary types.

The primary form is characterized by an essentially normal histopathology of the skin. It is divided based on the absence or presence of underlying neurological and ophthalmological abnormalities into essential and non-essential, respectively. The abnormalities may include impaired cognition, learning difficulties, cerebral palsy, schizophrenia, microcephaly, deafness, cataracts, retinitis pigmentosa and strabismus.

Secondary cutis verticis gyrata may occur secondary to various diseases. These include:

- Endocrine diseases (acromegaly, myxedema, Grave's disease, diabetes mellitus)
- Hereditary disorders (pachydermoperiostosis, Turner syndrome, Noonan syndrome, Ehlers–Danlos syndrome, Beare–Stevenson syndrome, Fragile X syndrome, Klinefelter syndrome, "Michelin tire baby" syndrome, tuberous sclerosis, hyperimmunoglobulin E syndrome)
- Inflammatory cutaneous diseases (eczema, psoriasis, Darier's disease, folliculitis, impetigo, erysipelas, atopic dermatitis, acne conglobata, acanthosis nigricans)
- Infections (syphilis)
- Benign tumors/infiltrates (dermatofibroma, cerebriform intradermal nevus, neurofibroma, neurinoma, collagenoma, focal mucinosis, amyloidosis, intraventricular ependymoma, cutaneous leiomyomatosis, cutaneous neurocristic hamartoma)
- Malignant tumors (fallopian tube carcinoma, infiltrating ductal carcinoma, angiosarcoma, malignant melanoma, acute myelogenous leukemia, acute monoblastic leukemia).

DOWLING–DEGOS DISEASE

Describe the clinical features of Dowling–Degos disease

Dowling–Degos disease is a rare autosomal dominant genodermatosis occurring due to a loss-of-function mutation in keratin 5 gene.

It is characterized by reticulate hyperpigmentation of flexural sites such as the neck, axilla, cubital fossa and groin and hence termed as reticulate pigmented anomaly of the flexures.

The pigmentation is typically symmetrical and progressive; it may become confluent, with a brown or black lace-like pattern. Comedo-like lesions may be seen on the trunk and face and pitted acneiform scars can occur at the angles of the mouth.

Enumerate other associated conditions occurring with Dowling–Degos disease

Dowling–Degos disease may overlap with acropigmentation of Kitamura and Haber's syndrome and can occur in association with hidradenitis suppurativa. Dowling–Degos disease is a benign condition; rarely, some tumors have been reported: squamous cell carcinoma, keratoacanthoma and a recent report of metastatic amelanotic melanoma.

Describe the histological features of Dowling–Degos disease

The histological features are characteristic; a distinctive acanthosis is seen and is characterized by an irregular elongation of thin branching rete ridges, with a heavy concentration of melanin at the tips. Follicular plugging and horn cysts may be present.

KERATOSIS FOLLICULARIS SPINULOSA DECALVANS

What is the inheritance of keratosis follicularis spinulosa decalvans?

Keratosis follicularis spinulosa decalvans was first described by Siemens in 1926 and has an X-linked recessive mode of inheritance. It occurs due to a missense mutation in the membrane-bound transcription factor peptidase site 2 gene which leads

to disturbed epidermal differentiation due to inhibition of cholesterol biosynthesis.

Describe the clinical features of keratosis follicularis spinulosa decalvans

A progressive cicatricial alopecia of the scalp, eyebrows and eyelashes starts in late childhood and remits by adolescence. It begins as follicular papules on the affected areas; there may be pustular flares and further progression to scarring alopecia. Focal plantar keratoderma may be present. Ocular abnormalities include photophobia, corneal opacities and blepharitis may occur. Oral manifestations include absent or conoid teeth, dental caries and enamel hypoplasia. Thickened dystrophic nails and high cuticles have been described.

What are the treatment modalities for keratosis follicularis spinulosa decalvans?

Topical keratolytic agents and emollients give symptomatic improvement. Antibiotics may be necessary during pustular flares of disease. Oral retinoids are effective in the early phase of the disease when active perifollicular infiltrate present. It must be continued for 6–12 months for optimum response.

ASCHER SYNDROME

What are the components of Ascher syndrome?

Ascher syndrome is characterized by blepharochalasis, progressive enlargement of the upper lip, and non-toxic goiter, but all the features may not be seen in every case. There may be inflammation and hypertrophy of labial salivary glands and accessory salivary glands.

Enumerate the differential diagnose of Ascher syndrome

Ascher syndrome is commonly confused with Melkersson–Rosenthal syndrome; other conditions being hereditary angioneurotic edema, early-onset dermatochalasis and acquired cutis laxa. Mounier–Kuhn syndrome can also have similar features, in addition to congenital tracheobronchomegaly.

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