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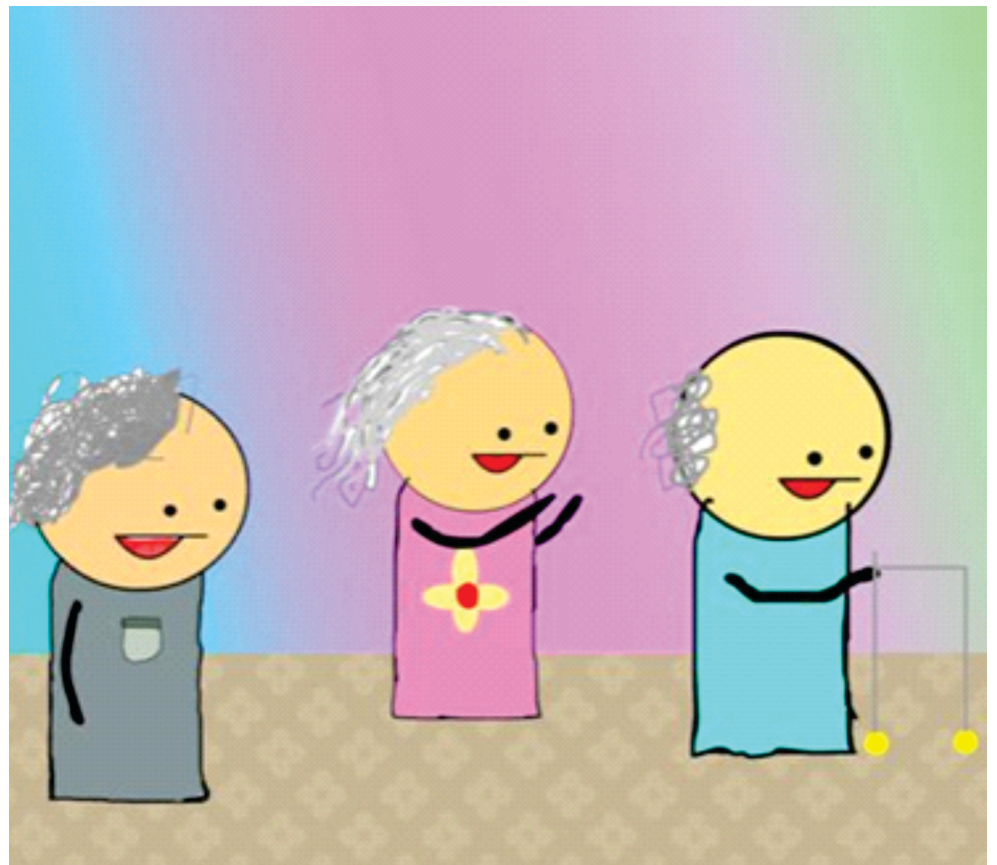
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IMMUNOSUPPRESSANTS IN GERIATRICS

Dr.Leelavathy Budamakuntla

Generally elderly patients are defined as those aged >65 years. This age group is more likely to have multiple comorbidities and are at increased risk of adverse drug reactions. Elderly patients are generally immunosenescent. Immunosenescence means reduced immune reactivity due to decline in naïve T-cells, accumulation of memory T-cells and alteration of B-cells causing a decrease in antibody response. Immunosenescence in elderly patients increases the risk of infections, malignancies, atherosclerosis and neurodegeneration when long term immunosuppressants are used.

Also, aging has an impact on the pharmacokinetics of the Immunosuppressive drugs. Renal drug excretion is often significantly reduced in the elderly regardless of comorbidities. Reduced GI motility and delayed gastric emptying may affect absorption of systemic drug usage. Reduction in lean body mass with relative increase in body fat affects distribution of the drugs. Reduction in renal and hepatic function impairs excretion of the systemic drugs.

Parameters like reduction in liver volume, blood flow, serum albumin concentrations and expression of CYP450 enzyme result in alterations in drug clearance. Responses seen in the elderly can be unexpected and exaggerated when compared to younger adults with similar characteristics. Certain factors like polypharmacy, non-adherence to medication, adverse drug reactions and drug interactions pose serious problems in the elderly.

IMMUNOSUPPRESSANTS :

These are the agents which act on cell division and have anti inflammatory effects. They are primarily used in elderly patients in the treatment of autoimmune diseases, solid organ transplants, psoriasis, bullous pemphigoid, pemphigus vulgaris, eczema, collagenoses, vasculitic disorders etc. Since the number of elderly patients receiving solid organ transplant is steadily increasing, there is a dire need to know about monitoring immunosuppressants in them.

Immunosuppressants have a narrow therapeutic index and hence therapeutic drug level monitoring is essential in elderly. The selection of immunosuppressive medication regimens in the elderly is complex as there are no specific guidelines as generally elderly people are excluded from the clinical trials.

Classification of immunosuppressants:

- Selective inhibitors of cytokine production & function: Cyclosporine, Tacrolimus, Sirolimus.
- Immunosuppressive antimetabolites: Methotrexate, Azathioprine.
- Antibodies(Biologicals): Adalimumab, Etanercept, Infliximab, Rituximab, Ustekinumab
- Corticosteroids: Prednisolone, Dexamethasone, Methylprednisolone.

Some of the important features of commonly used immunosuppressants in elderly are listed below:

CORTICOSTEROIDS

- Most commonly used immunosuppressants with nonspecific anti-inflammatory property inhibiting multiple steps in immune activation.
- Used most commonly in bullous disorders, eczema, autoimmune disorders, vasculitis.
- Main side effects: weight gain, hypertension, hyperlipidemia, osteopenia, hyperglycemia, poor wound healing, Myopathy, Cataracts, Peptic ulcer. Corticosteroids have the strongest diabetogenic potential, which is dose dependent.
- The effects of ageing on the pharmacokinetics of prednisolone are unknown.

CYCLOSPORINE:

- Derived from the fungus *Tolypocladium inflatum* - specific inhibitor of T-cell mediated immunity.
- Dosage & Uses: - 3.5-5mg/kg body weight Used in conditions like Psoriasis (erythrodermic, arthropathic, pustular, recalcitrant), collagenoses, lichen planus, Behcet's disease, Sweet's syndrome, pyoderma gangrenosum.
- Adverse effects – nephrotoxicity, hepatotoxicity, anorexia, gum hypertrophy, hypertension, hyperlipidemia, hirsutism, osteoporosis, tremors, seizures.
- Monitoring:
 - Blood pressure – If there is an increase in BP (diastolic > 90mmHg or systolic > 140mmHg), BP measurement - repeated after two weeks. If BP is still elevated reduce the dose by 25-50%.
 - Renal function – If creatinine levels are >30% of basal levels – repeat test after two weeks. If levels still remain high, dose should be reduced by 1mg/kg.
 - After one month of administration of the reduced dose, creatinine levels are reevaluated:
 1. If returns to normal, cyclosporine therapy can be continued.
 2. If still high, treatment should be interrupted.
- Cyclosporine if used for more than one year – nephrologist evaluation for fibrosis (by kidney biopsy) should be taken.
- The pharmacokinetics of medications, particularly calcineurin inhibitors (CNIs) may be altered in older patients. Doses that are similar to those recommended for younger patients may result in higher drug concentrations. This is because of reduction in metabolism from CYP3A4 isoenzymes and reduced P-glycoprotein activity.
- Many authors suggested that in elderly patients a significantly larger proportion of the whole blood cyclosporine concentration may be located at the site of action (within the T-lymphocyte) indicating that in this population it might be safe to aim for an even lower target level than current guidelines.
- Elderly patients receiving CNIs or mycophenolate should consistently receive the same brand of immunosuppressant once they are stabilized
- Interchanging brands is likely to result in variability of immunosuppressant levels, potentially exposing the patient to an increased risk of adverse effects.

CYCLOPHOSPHAMIDE:

- Nitrogen mustard alkylating agent synthesized in 1958
- Approved by the FDA for the treatment of mycosis fungoides
- Other indications: Vasculitis (especially Wegener's granulomatosis); bullous disorders; neutrophilic dermatoses; collagenoses; infiltrative diseases, histiocytosis X.
- Adverse reactions: Hematologic reactions (leukemia, lymphoma, pancytopenia), Gastrointestinal (hepatotoxicity, nausea, vomiting) and Genitourinary (bladder cancer, hemorrhagic cystitis). Usually BPH (Benign Prostatic Hyperplasia) is common in elderly male patients and there will be chance of urinary retention which might increase the chance of bladder side effects due to drug accumulation although it is very rarely reported.
- Drug interactions: cimetidine, allopurinol, and chloramphenicol can increase serum levels of cyclophosphamide. Chlorambucil and mechlorethamine have cross reaction and may lead to hypersensitivity to cyclophosphamide.
- No proper data is available on dosage modulation in elderly patients.

METHOTREXATE:

- Chemical analogue of folic acid, acts by competitively and irreversibly inhibiting dihydrofolate reductase.
- Used in psoriasis (FDA approved in 1971), bullous disorders (bullous pemphigoid; pemphigus vulgaris and foliaceus), Sézary syndrome, mycosis fungoides, collagenoses (lupus erythematosus; dermatomyositis; scleroderma), Vasculitis and neutrophilic dermatoses.
- Adverse effects – Short-term: Hematologic effects – pancytopenia; Long-term: hepatic alterations.
- Generally there is age-related decline in renal function at approximately 10% per decade of increasing age.
- The metabolism and excretion of methotrexate is affected by age resulting in toxicities as reported in many cases.
- Close monitoring of renal function in the elderly is essential during methotrexate therapy, as many methotrexate-related adverse effects can be related to impaired renal function.

AZATHIOPRINE:

- Prodrug of mercaptopurine (purine analog)
- First drug to be used for immune suppression after transplantation.

- Adverse effects – bleeding gums, chest pain, fever or chills, painful urination, sore throat, swollen joints, leukopenia, bone marrow suppression, hepatic dysfunction, risk of carcinoma. Pulmonary fibrosis can occur idiosyncratically.
- Drug interactions:
 - Allopurinol - severe myelotoxicity. If both drugs need to be used in combination, the dose of azathioprine should be reduced by 25-30%. Captopril may increase the risk of leucopenia if used simultaneously.

MYCOPHENOLATE MOFETIL:

- A semi-synthetic derivative of mycophenolic acid, acts by inhibiting Inosine monophosphate dehydrogenase.
- Used as steroid sparing agent in pemphigus vulgaris, pemphigus foliaceus, bullous pemphigoid, pyoderma gangrenosum, vasculitis.
- Side effects Leucopenia, headache, gastrointestinal disturbances, hypertension, bone marrow suppression. It can also cause reactivation of CMV.
- Elderly patients have higher apparent clearance of mycophenolate, which contradicts our general understanding of the effects of aging on the pharmacokinetics of a drug.
- Elderly patients require higher doses of mycophenolic acid (MPA) when compared with younger patients. The reason may be that MPA is strongly bound to serum albumin, and lower albumin levels in elderly patients result in increased clearance of unbound MPA.

VACCINATION IN ELDERLY PATIENTS ON IMMUNOSUPPRESSANTS:

- Vaccinating immunocompromised patients can be challenging as they may have a reduced response to vaccines, as well as reduced protection from previous vaccinations.
- Immunosuppressed patients may need extra doses of inactivated vaccines to optimize protection against specific diseases.
- Vaccination should ideally be undertaken prior to immunosuppressive therapy to improve the immune response.
- Administration of live vaccines – such as measles, mumps and rubella (MMR), varicella and zoster vaccines – to immunocompromised hosts is generally contraindicated.
- Mildly immunosuppressed patients, such as those taking conventional disease modifying antirheumatic medications for example low-dose methotrexate, azathioprine or corticosteroids can receive live vaccines.
- Otherwise, patients should ideally wait four weeks before starting immunosuppression after receiving a live vaccine to start immunosuppressants.

Conclusion:

- Immunosuppressive drugs are extremely valuable tools in the therapeutic arsenal of dermatologists when used wisely.

➤ ***Important aspects to be followed while prescribing:***

- Immunosuppressants used must have clearly defined indication.
- Patient education regarding safety and proper use.
- Maintain records containing complete medication review, including OTC and herbal medications.
- Therapeutic endpoints and ADR (Adverse Drug Reactions) must be monitored.
- Identify the vulnerable elderly patients more likely to experience adverse drug events and educate them.
- Use an evidence-based approach to guide prescribing decisions in the elderly.
- Implement office-based procedures to safeguard prescribing in at-risk elderly patients.
- Close surveillance and collaboration is necessary by all practitioners involved in their care.
- In this way, elderly patients can be offered better Quality of Life (QOL) with fewer or attenuated risk.

Polypharmacy in Elderly

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“One of the first duties of the physician is to educate the masses not to take medicine.”
“The good physician treats the disease; the great physician treats the patient who has the disease.”

“The person who takes medicine must recover twice, once from the disease and once from the medicine.”

William Osler

Introduction:

Polypharmacy is a global health issue, particularly in elderly. It lacks a universally acceptable definition. The General consensus is “Concurrent use of 5–9 drugs” constitutes polypharmacy. It can increase the risk for adverse drug events. Sometimes it may be a necessary evil.

Types:

- **Hyperpolypharmacy-** Consumption of ≥ 10 pills
- **Oligopharmacy-** consumption of ≤ 5 pills
- **Appropriate Polypharmacy:** Rational/Evidence based
- **Inappropriate:** Irrational
- **Same class:** Use of 2 or more drug from same class for same disease
- **Multi-class:** Use of more than one medication for same symptom cluster
- **Adjunctive:** Use of one medication to treat side effect of another medication
- **Augmentation:** Use of one medication in lower dose and another medication from different class in higher dose

Risk Factors:

Comorbidity and polypharmacy significantly increase the risk of ADRs - 13% (2 drugs); 58% (5 drugs); 82% (7 or more drugs). Others include:

- Demographic shift; increasing Geriatric population
- Multiple comorbid conditions (80% in aged >80)
- More reliance on pills/Changing lifestyle
- Multiple physicians consults
- Easy access to pharmacies/chemist
- False Assumption that all medications needs to be continued once started
- Vitamins and many OTC products not considered drug

Consequences:

- Adds to the expense of therapy
- Poor Adherence/ Decreased compliance
- Drug-drug interactions
- Adverse drug reactions
- Poor quality of life/ Outcomes

Management: Involves 2 important strategies

1, Avoidance of Prescribing cascade

An important cause of polypharmacy. Defined as “The inability to distinguish drug-induced symptoms (ADRs) from a definitive primary medical condition, leading to addition of yet another drug to treat the symptoms, which increases chances of ADRs”

2. Deprescribing: The process of tapering, stopping, discontinuing or withdrawing drugs, with the goal of managing polypharmacy and improving outcomes.

Preventing Polypharmacy: by adopting “ TIDE and SAIL concept” which includes:

- **Simple:** Use simple regimen with once or twice a day which can treat multiple indications to reduce pill burden
- **Adverse effects:** Choose safer medications with broad therapeutic indices. Identify medications that are treating adverse effects of other medications
- **Indication:** Ensure each medication has an indication and a defined, realistic therapeutic goal
- **List:** Note down the name and dose of each medication in the chart and look for potentiality of ADI/ADR
- **Time:** Allow sufficient time to address and discuss medication issues
- **Individualize:** Select drug based on pharmacokinetic and pharmacodynamic principles and patient's renal or hepatic function. Adopt “start low, go slow” policy
- **Drug-drug and drug-disease interactions:** Avoid combining potentially dangerous interactions such as those leading to torsades de pointes
- **Educate:** Educate the patient and caregiver. Discuss expected medication effects, potential adverse effects, and drug-drug interactions and monitoring parameters

Premalignant lesions in elderly

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Ageing causes a decline in function of human skin, while medical conditions, drugs and environmental irritants add to the compromised skin and predispose it to certain conditions. Superimposed on the physiological ageing of skin, chronic sun exposure makes matter worse. Skin neoplasia, benign, premalignant or malignant, are more common in elderly. It is important to identify benign conditions and lesions with a malignant potential so that timely treatment can prevent serious malignancies.

These lesions are classified for sake of simplicity into those of epithelial and non-epithelial origin.

Epithelial Origin	Non Epithelial Origin
<ol style="list-style-type: none">1. Actinic keratosis2. Bowens disease3. Leukoplakia4. Erythroplakia5. Buschke –Lowenstein tumor6. Erythroplasia of Queyrat7. Keratoacanthoma8. Disseminated superficial actinic porokeratosis9. Erosive LP	<ol style="list-style-type: none">1. Lentigo maligna2. Lichen sclerosis et atrophicus3. Sebaceous nevus4. Extramammary Paget 's disease

Premalignant lesions of Epithelial Origin

1. Actinic keratosis(AK):

It is proliferation of atypical epidermal cell due to the ultra violet rays (UVR). It occurs due to high cumulative exposure to UVR due to outdoor work, in fair skin and underlying immunosuppression. It occurs on sun exposed body area i.e. balding scalp, head, (Fig 1) neck, forearms, dorsal aspect of hand in males and on dorsal aspect of legs in females. Patient presents with 2 to 6 mm flat, gritty, erythematous and scaly papules along with signs of photo damage such as solar lentigenes and wrinkling. Actinic cheilitis (AC) commonly affect lower lip and is confluence of AK. It presents as scaly, red, chapped and eroded lip. Diagnosis of both AK and AC are done by biopsy. AK and AC are premalignant lesions which can progress to squamous cell carcinoma (SCC). Cryotherapy, ablative lasers, imiquimod, 5FU and photodynamic therapy are the modalities of treatment available. Use of sunscreens decrease the incidence and prevalence of AK.



Fig 1: Erythematous well defined plaques over scalp

Bowen's disease (BD):

BD is SCC in situ and affects males more than female greater than 60 years of age. BD presents as asymptomatic to pruritic erythematous plaque to nodules with scaling, crusting on sun-exposed part like hand, neck, ears, cheeks, balding scalp, lower limb(Fig 2) and upper limb. On oral mucosa and anogenital region, it is called erythroplakia and erythroplasia of Queyrat respectively. UVR, human papilloma virus(HPV), immunosuppression, ionising radiations and arsenic exposure are etiological factors. Biopsy is required for diagnosis. Topical 5- fluorouracil(5-FU), cryosurgery, electrosurgery, surgical excision and photodynamic therapy(PDT) are used for treatment. It rarely transforms into SCC but carries a higher risk in immunocompromised patients.



Fig 2: Well defined, minimally elevated, flat plaque present over left leg

3. Leukoplakia:

Leukoplakia is white lesion on oral mucosa which cannot be rubbed off and of unknown etiology or may have a definite cause(Fig. 3). It is potential malignant lesion could lead to SCC. Erythroplakia and leukoplakia have same clinical spectrum. Etiological factors are consuming tobacco product, alcohol abuse, history of previous or premalignant lesions, and infection with certain human papillomavirus. It most commonly occurs in males at or after 40 years. It is of two type homogenous and non-homogeneous. Presence of epithelial dysplasia, large size, location at floor of mouth, nonhomogeneous, female gender, chronic leukoplakia have high chance of malignant transformation. It will regress on its own when risk factors are removed. If not, surgical excision is treatment of choice.



Fig 3: Homogenous white plaque over lower lip

4. Erythroplakia:

It is red coloured macule to plaque on oral mucosa(Fig 4). Etiological factors are similar to leucoplakia. When associated with leukoplakia it is called erythroleukoplakia. It is diagnosed by exclusion and so should be differentiated from atrophic lichen planus, lupus erythematosus, erythematous candidiasis, pemphigus, cicatricial pemphigoid, Kaposi sarcoma and chronic contact or allergic contact dermatitis. It can transform to SCC. It can be removed by excision and CO2 laser.



Fig 4: Persistent Erythematous plaque over soft palate

5. Buschke-Lowenstein tumour:

It is also called as giant condylomata acuminatum (Fig 5). It is asymptomatic, papillomatous lesions occur at anogenital and perineal area due HPV virus. Maceration and secondary infection are commonly associated complications. Recurrence after excision is common. Topical podophyllin, cryotherapy, excision, CO₂ laser ablation, radiotherapy are the common treatment modalities used.



Fig 5: Large irregular, firm , hyperkeratotic plaque perianal region

6. Erythroplasia of Queyrat (EQ):

EQ or Bowenoid papulosis (BP) and BD are penile interstitial neoplasia (PIN). It is analogous to cervical, vulvar, anal interstitial neoplasia. Poor hygiene, smegma, trauma, friction, ultraviolet light, HPV-16 and 18 are risk factor for EQ. It is located on glans and prepuce and presents as erythematous, velvety plaque associated with pruritus. Excision of lesion is definitive treatment but topical cidofovir and bleomycin, PDT, radiotherapy, CO₂ laser can be used.

7. Keratoacanthoma (KA):

According to some authors KA is considered a variant of SCC and by others to represent benign tumors (i.e. pseudomalignancy). The exact nosology is still uncertain. It occurs on sun exposed part of body such as head, neck and extremity. It presents as papules which grow rapidly to form crateriform nodule with keratotic core in weeks then resolve slowly over month to atrophic scar. Other clinical variants are solitary, multiple, grouped, keratoacanthoma centrifugum marginatum, giant, subungual, palmoplantar, intraoral, multiple spontaneously regressing, multiple non-regressing and generalized eruptive forms. Multiple KAs have been associated with chemical exposures, immunosuppression, BRAF inhibitors, and HPV infection. It is seen in Muir–Torre syndrome and Ferguson–Smith syndrome. Cryotherapy, curettage and cautery, excision, radiotherapy, oral acitretin, methotrexate, cyclophosphamide are treatment modalities used.

8. Disseminated superficial actinic porokeratosis (DSAK):

It is inherited as autosomal dominant (AD). It present as pink to brown papules and plaques with peripheral scales. It arises in sun-exposed sites, especially the extensor forearms and shins; measuring from a few mm to 1 cm in diameter. It is more common in Caucasians and rare in blacks. It occurs in third and fourth decades. It is associated with hepatitis C infection or systemic lupus erythematosus. Histopathology shows coronoid lamella. 5 fluorouracil, calcipotriol, cryotherapy, dermabrasion, CO₂ laser, oral isotretinoin and acitretin can be used for treatment. In the old age it may get transformed to BCC or SCC. So constant monitoring is a must.

9. Erosive lichen planus (LP)

It is a variant of LP. It is seen on feet, scalp, oral mucosa (Fig 6), nails. It can present as chronic, painful, bullous lesions. Rarely it can develop into SCC.

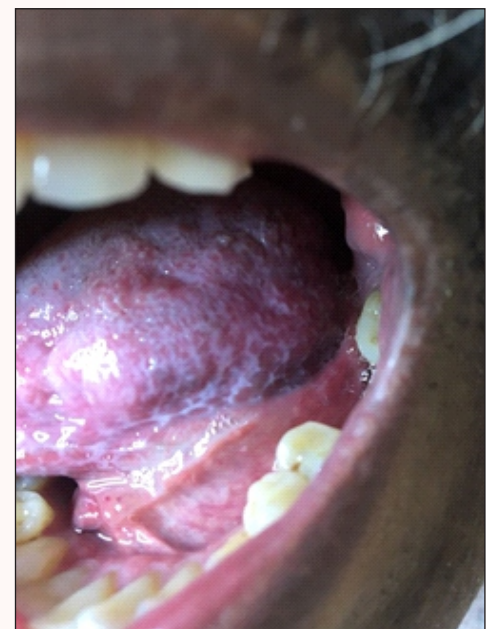


Fig 6: Oral erosive lesions with violaceous streaks

Premalignant lesions of Non-Epithelial Origin

1. Lentigo maligna (LM):

It is melanoma in situ. When it extends radially and become invasive then it is called lentigo maligna melanoma (LMM). Age of onset is 7 to 8 decades, uncommon before 40 years, presents on sun exposed parts face, cheeks, nose, scalp and ear. It is due to cumulative sun exposure. It slowly enlarges to become brown freckle like macules with irregular shape and different shades. LMM have high recurrence after excision

2. Lichen sclerosus et atrophicus (LSA):

It is an inflammatory dermatosis. Etiology of LSA is unknown but commonly associated with autoimmune disorder and HLA II DQ7. More common in women than men with bimodal onset i.e. prepubertal and post-menopausal. It affects genital(Fig 7) and extra genital sites. At perineum it forms figure of 8 around anus and vulva. It affects skin at genital area but mucosa is spared. It has 4-5% risk of transformation of SCC. In this condition there is inflammation and altered fibroblast function. Ultra-potent topical and intralesional steroids, calcineurin inhibitors and PUVA can be used for treatment.



Fig 7: Hypopigmented sclerotic plaque over prepuce with phimosis

3. Sebaceous nevi:

It is congenital hamartoma. It goes through three stages. In prepubertal stage multiple underdeveloped sebaceous glands and hair follicles are seen. In pubertal stage there is massive growth of the sebaceous glands and maturation of apocrine glands and malformed hair roots are seen as buds of basaloid cell. In third stage it undergoes benign and malignant changes. Syringocystadenoma papilliferum is the benign appendageal tumour and basal cell carcinoma the malignant tumour. Surgical excision, CO₂ laser and PDT can be used for treatment.

4. Extramammary Paget's disease

It is a rare disease, of sixth to eight decades occurring at areas with abundant apocrine gland such as vulva, perineal, scrotal, perianal, pubic(Fig 8) and penile skin. It presents as erythematous, well demarcated plaques. It may become erosive, ulcerated, scaly or eczematous. Treated by surgical excision.



Fig 8: Pruritic, erythematous, marginated eczematous plaque

Conclusion

Ultraviolet radiation is the major etiological factor for the development of skin cancer. Regular scrutiny of the skin will ensure early identification of dermatological problems and implementation of a good skin care plan can compensate for failing physiologic function.

SIG LITERATURE-REVIEW

Vignesh Narayan R, Hitaishi Mehta, Anuradha Bishnoi

With advances in healthcare and increased life expectancy, geriatric population continues to increase. Clinical presentation, prognosis and management of certain dermatoses in this population (differ/s) from other groups and the current literature focusing on elderly continues to expand. Following is a summary of some important articles published concerning geriatric dermatology over past two years.

1. **“Survival, disease progression and prognostic factors in elderly patients with mycosis fungoides and Sézary syndrome: a retrospective analysis of 174 patients”**

(Lebowitz E, Geller S, Flores E, Pulitzer M, Horwitz S, Moskowitz A, et al. Survival, disease progression and prognostic factors in elderly patients with mycosis fungoides and Sézary syndrome: a retrospective analysis of 174 patients. *J Eur Acad Dermatol Venereol* 2019; 33:108–14).

Advanced age at diagnosis is considered a poor prognostic factor in mycosis fungoides (MF) and Sézary syndrome (SS). In order to assess the validity and find additional prognosticating factors, the authors studied a group of 174 elderly patients diagnosed with MF/SS between 1992 and 2015 at a single referral cancer centre in the United States. They found that of 174 elderly patients, 76.4% were diagnosed with early-stage (clinical stages IA-IIA) and 23.6% with late-stage MF/SS (IIB-IV). Advanced age was associated with poor overall survival, but not with disease-specific survival (DSS) or progression-free survival (PFS). Increasing clinical stage, T and B classifications, elevated lactate dehydrogenase (LDH) levels and development of large cell transformation (LCT) were significant predictors of poor survival or disease progression. Patients with early-stage MF and <10% total skin involvement (T1 classification) or patch-only disease (T1a/T2a) showed better PFS with no observed disease-specific mortality. Folliculotropic MF was associated with poor DSS in patients with early-stage disease.¹

2. **“Functional status and survival in patients ≥85 years of age who have keratinocyte carcinoma: A retrospective cohort study**

(Vora NB, Connolly KL, Dusza S, Rossi AM, Nehal KS, Lee EH. Functional status and survival in patients ≥85 years of age who have keratinocyte carcinoma: A retrospective cohort study. *J Am Acad Dermatol* 2020; 83:463–8.)

Functional status assessment may help estimate which patients ≥85 years of age will benefit from surgical treatment for keratinocyte carcinoma (KC), but predictive value for short-term survival in this population has not been determined. In order to assess this, a retrospective cohort review of 238 patients ≥85 years of age who presented for the management of KC between 2010 and 2015 was undertaken, functional status being assessed with the Karnofsky Performance Scale (KPS) and Katz Activities of Daily Living (ADL) index. Lower functional status scores of KPS ≤40 and Katz ADL ≤4 was associated with 37% and 53% survival at 2 years, respectively. Functional status should be considered during shared decision-making for elderly individuals who are seeking treatment for KC.”²

Editorial comments

Above two studies emphasize the importance of the assessment of the overall functional status when evaluating

elderly people having skin malignancies like mycosis fungoides and keratinocytic carcinomas. We do come across such patients, and though the specific disease related markers like folliculotropism and large cell transformation in mycosis fungoides and morpheiform and basosquamous features in basal cell carcinomas, do affect the prognosis and outcome, we should use appropriate clinical tools to evaluate the general performance status, which determines mortality even in the absence of the poor disease-related markers, and has bearing on the treatment options that we decide to opt for in the geriatric population. Very early stage mycosis fungoides can also be just observed using 'wait and watch' strategy instead of administering any active treatment (Bishnoi A, Kumar S, Vinay K. Stage IA mycosis fungoides: When not to treat? *J. Am. Acad. Dermatol.* 2020; 82:e17–8). Similarly, keratinocytic carcinomas can be treated using radiotherapy instead of subjecting patients having a poor performance status to extensive surgical procedures and chemotherapy regimens.

3. “Scabies outbreaks in ten care homes for elderly people: a prospective study of clinical features, epidemiology, and treatment outcomes”

(Cassell JA, Middleton J, Nalabanda A, Lanza S, Head MG, Bostock J, et al. Scabies outbreaks in ten care homes for elderly people: a prospective study of clinical features, epidemiology, and treatment outcomes. *Lancet Infect Dis* 2018; 18:894–902)

This prospective observational study was performed in residential care homes for elderly people in southeast England that reported scabies outbreaks to Public Health England health protection teams. In ten outbreaks between Jan 23, 2014, and April 13, 2015, 230 residents were examined. Median age was 86•9 years (IQR 81•5–92•3), 174 (76%) were females, and 157 (68%) had dementia. Of all, 61 (27%) residents were diagnosed with definite, probable, or possible scabies, of whom three had crusted scabies. Physical signs differed substantially from classic presentations. Of the 61 people diagnosed with scabies, 31 (51%) were asymptomatic, and only 25 (41%) had burrows. Mites were visualised with Dermatoscopy in seven (11%) patients, and further confirmed by microscopy in three (5%). Also, 35 (57%) cases had signs of scabies only on areas of the body that would normally be covered. Dementia was the strongest and the only risk factor identified (odds ratio 2•37 [95% CI 1•38–4•07]).

4. “Non-bullous pemphigoid: Insights in clinical and diagnostic findings, treatment responses, and prognosis” (Lamberts A, Meijer JM, Pas HH, Diercks GFH, Horváth B, Jonkman MF. Nonbullous pemphigoid: Insights in clinical and diagnostic findings, treatment responses, and prognosis. *J Am Acad Dermatol* 2019; 81:355–63.)

Nonbullous pemphigoid is characterized by the absence of blisters causing considerable delay in diagnosis. In order to describe its characteristics, a retrospective review study of medical records of 69 patients was undertaken. The diagnosis of pemphigoid was based on meeting 2 of the following 3 criteria: (1) pruritus, (2) positive direct immunofluorescence microscopy, or (3) positive indirect immunofluorescence microscopy on salt-split skin. The mean delay in diagnosis was 29 months. Skin examination most often showed pruritic papules/nodules (37%) or pruritus without primary skin lesions (22%). Histopathologic findings were mainly nonspecific. Results of direct and indirect immunofluorescence microscopy were positive in 60% and 69%, respectively. During follow-up, blisters formed in 17%, which was associated with a positive indirect

immunofluorescence microscopy ($P = .014$) and a positive BP180 immunoblot result ($P = .032$). The Kaplan-Meier estimates of mortality at 1, 2, and 3 years were 14%, 34%, and 46%, respectively, with an 8.6-fold increased all-cause mortality risk.

Editorial comments

Pruritus is a significant issue in elderly people. These two articles convey a very important message, that in elderly people presenting with chronic pruritus, scabies and non-bullous pemphigoid (NBP) should always be considered. Scabies can present with an atypical history, morphology and distribution (absence of lesions in web spaces, a site commonly involved in younger people). A strong clinical suspicion in presence of primary lesions (papules, nodules, vesicles and burrows) and secondary lesions (excoriations) can help to diagnose scabies and provide relief to the patients and their families. Importantly, around 50% of these patients did not report itching or any other skin symptoms, especially those having dementia. Dermatoscopy and microscopy can also be utilized in difficult cases. NBP is again an important though rare cause of pruritus in elderly people, and can present with very non-specific clinical features. In presence of clinical suspicion, immunofluorescence studies can be carried out to further substantiate the diagnosis, and initiate appropriate treatment.

5. “Biologic Treatment in Elderly Patients with Psoriasis: A Systematic Review

(Sandhu VK, Ighani A, Fleming P, Lynde CW. Biologic Treatment in Elderly Patients With Psoriasis: A Systematic Review. *J Cutan Med Surg* 2020; 24:174–86.)

Elderly patients often have multiple comorbidities and immunosenescence making biologics a tempting option in the management of psoriasis. In order to study the safety and efficacy of biologics in elderly patients with moderate-to-severe psoriasis, a systematic review was undertaken. MEDLINE, Embase, the Cochrane Library, and clinical trial databases were searched. Studies were included if elderly patients were the main population of interest or were a separate subgroup in their analysis. Eighteen articles met inclusion criteria after screening. Across all biologic classes, efficacy for biologics between nonelderly adult patients and elderly patients was similar. Adverse events (AEs) and infections occurred at a similar frequency between both groups. However, serious AEs and treatment discontinuation were more common in the elderly.⁶

6. Efficacy and safety of dupilumab in atopic dermatitis in elderly patients: a retrospective study

(Napolitano M, Fabbrocini G, Scalvenzi M, Blasio C, Stingeni L, Patrino C. Efficacy and safety of dupilumab in atopic dermatitis in elderly patients: a retrospective study. *Clin Exp Dermatol* 2020; ced.14260).

This retrospective observational study reviewed the elderly (≥ 65 years) patients with moderate-to-severe AD treated with dupilumab administered subcutaneously at label dosage (600 mg induction dose, followed by 300 mg every 2 weeks). Demographic and clinical data for each participant was assessed at baseline and at week 16. Disease severity was evaluated using EASI, visual analogue scale for pruritus (VAS-P) ranging from 0 to 10 (where 0 = ‘does not itch at all’ and 1 = ‘itch is worse than ever’) and Dermatology Life Quality Index (DLQI). Of the 30 patients, 22 (73.3%) had adult-onset AD, whereas in the other 8 (26.7%), the AD had persisted since childhood.

Throughout the follow-up period, there was a statistically significant reduction in mean EASI from 27.2 ± 7.26 vs. 2.5 ± 3.26 , in VAS-P from 8.5 ± 1.54 vs. 0.9 ± 1.42 and in DLQI from 20.9 ± 4.96 vs. 5.03 ± 3.71 ($P < 0.001$ for all). Dupilumab shows both optimal efficacy and a favourable safety profile in patients aged ≥ 65 years.⁷

7. “The efficacy and safety of phototherapy in geriatric patients: a retrospective study”

(Bulur I, Erdogan HK, Aksu AE, Karapinar T, Saracoglu ZN. The efficacy and safety of phototherapy in geriatric patients: A retrospective study. *An Bras Dermatol* 2018; 93:33–8)

A retrospective study including 95 patients of 65 years of age and older who were treated in phototherapy unit of the authors between 2006 and 2015 was conducted to see the efficacy and safety. Phototherapy was administered to 28 (29.5%) patients for mycosis fungoides, 25 (26.3%) patients for plaque type psoriasis, 12 (12.6%) patients for palmoplantar psoriasis, 12 (12.6%) patients for generalized pruritus, and 18 (19%) for other dermatoses. Of the patients, 64.2% had received a narrowband UVB (NB-UVB), 21.1% oral psoralen UVA (PUVA), and 14.7% local PUVA treatment. A complete response was achieved in 76.9-85.7% of the mycosis fungoides and in 73.71-100% of the psoriasis vulgaris patients treated with NB-UVB and PUVA, respectively. All the patients with generalized pruritus were treated with NB-UVB, and 80% of these patients achieved significant improvement. The erythema rate was found to be 0.43% per session for NB-UVB treatment and 0.46% per session for PUVA treatment as a side effect.⁸

Editorial comments

With an increasing life-expectancy, the number of elderly patients having psoriasis, mycosis fungoides, eczema and non-specific pruritus is going to rise. These three articles suggest that the biologics and phototherapy can be utilized as therapeutic options, when concomitant medications and co-morbidities exclude the usage of traditional immunosuppressants. A close follow-up, and appropriate increments in dosages can help to diagnose the adverse effects earlier when these do occur. Etanercept and secukinumab appear to have lesser adverse effects. Dupilumab can be used for severe atopic and endogenous eczemas. Phototherapy has an advantage of avoiding systemic immunosuppression and can be administered for a variety of dermatoses. The phototherapy cabins and areas should have necessary provisions for elderly people, like appropriate waiting area, comfortable chairs, lightening and supportive staff etc.

Serum Vit D estimation in geriatric population and disorders associated with hypovitaminosis D : A cross sectional study

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Vit D is a hormone with multiple physiologic functions. Medical literature have recently focused attention on the influence of Vit D on various aspects of health. In skin calcitriol synthesised in keratinocytes can regulate their growth/differentiation/apoptosis and other biological processes. Vit D insufficiency affects almost 50% Of the population world wide. This is the most under recognized nutritional deficiency.¹ There was a misconception that “in India, people do not have Vit D deficiency” because of plenty of sunshine available.²

Vit D estimation has not been done widely as it is a relatively expensive test.

A cross sectional study was undertaken to determine serum [25{OH}]Vit D level in different age groups and to assess the clinical spectrum of diseases present in those with Vit D deficiency. The patients were categorized as having severe deficiency(<10 ng/ml), deficiency(10 ng/ml to <20 ng/ml), insufficient(20 ng/ml to <30 ng/ml) and adequate level(≥ 30 ng/ml).

Two hundred and fifty patients were seen of which 76 were in geriatric age group. Out of the whole group, 53 had severe vit d deficiency, 126 were deficient, 55 had vit D insufficiency and 16 had adequate levels. Of the 76 geriatric patients 11 had severe, 37 had deficiency, 19 had insufficiency and 9 had adequate levels. Table 1 shows the serum Vit D level deficiency categories in geriatric population above the age of 60 years .

Table 1. Geriatric patients and their Vit D status

Total number	Number above age 60	Severe def	Deficiency	Insufficiency	Adequate
250	76	11(14.4%)	37(48.6%)	19(25%)	9(11.8%)

There found a clinical spectrum of various disorders in these 250 patients and their correlation with Vit D level status is shown in Table 2.

Table 2. Clinical disorders associated with low Vit D level

Diseases	Severe def	Deficiency	Insufficiency	Adequate
Dyslipidemia	3/53	24/126	15/55	3/16
Diabetes mellitus	8/53	35/126	10/55	2/16
Dermatological disorders	4/53	14/126	3/55	1/16
Cardiovascular diseases	5/53	12/126	6/55	0/16

Discussion

The main form of vit D is D3. It is synthesised in skin with UV B . 25-OH Vit D level is the nutritional indicator of vit D. It shows the best estimate of vit D status due to its long serum half-life(approx 3 weeks).But Cholecalciferol has short half-life, so that serum level depends on recent sunlight exposure and Vit D ingestion.

Associations have been observed between systemic diseases and dermatological diseases with vit D level:

- Oral Vit D improves metabolic syndrome and cardiovascular diseases which may also be associated with psoriasis.
- Rickets and Atopic dermatitis
- Vit D has an important role in vitiligo. Probably because of its antioxidation effects, its anti apoptotic effect, modulation of T cell activity. Vit D may have effect in protecting epidermal melanin unit. It may take part in melanin synthesis.
- Vit D has an established role in psoriasis through effect on epidermis & keratinocyte proliferation. It inhibits inflammatory mediators-IL 17,IL 8.
- Inhibition of fibroblasts by vit D can give some favourable effect in keloid.

Factors that regulate Vit D level are :

1. Melanin
2. Clothing
3. Dietary habits
4. Sun screens

Causes of vit D deficiency are:

1. Decreased synthesis because of skin pigmentation,sun screens, cloth
2. Geography-latitude,season
3. Decreased intake
4. Malabsorption
5. Decreased synthesis or increased degradation.

Conclusion:

It is essential to aim to ensure adequate levels of vit D particularly in geriatric population as it has important systemic and dermatological ramifications

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HOLISTIC ADJUVANT MANAGEMENT OF XEROSIS AND ASSOCIATED PROBLEMS OF GERIATRIC PATIENTS, ALONG WITH REGULAR TREATMENT

Prof. Rathindra Nath Dutta

Ageing is associated with structural and functional changes in the skin, causing thinning of the epidermis and dermis, fragmentation of collagen and elastic fibres and decreased cell healing and DNA repair. There is also a decrease in melanocytes and reduced function of sebaceous glands as well as a decrease in skin lipids, vascularity and supporting structures.

Thus some inevitable changes such as dryness, wrinkling, and laxity of the skin, and atypical presentations of dermatologic diseases are observed in elderly patients [1,2]

Xerosis or dryness of skin is one of the most common skin change that we see in elderly. Epidemiological studies conducted in nursing home populations have reported 30 to 75% prevalence of xerosis in the elderly [3,4,]. Pruritus in the elderly is most commonly associated with dry skin or xerosis.[5].

It is very important to recognise that ameliorating xerosis in elderly will go a long way in successfully treating several of their dermatoses. Some of the helpful measures are outlined below:

1. The first method that should be taken when treating xerotic eczema is attempting to re-hydrate the dry skin. Use of humidifier, bathing/showering (less frequently in warm water) will help.
2. Mild soaps should be used to prevent further irritation [6]
3. Avoiding scratching the affected area and applying anti-itch or moisturizing lotion frequently would also help in reducing dryness.
4. If the skin becomes inflamed or cracked, mid- to high-potency corticosteroids can be used.[7] A study published in 2005 found positive results from soaking the affected area in water for twenty minutes and then applying mid- to high-strength corticosteroid ointment.[8]

Hydrotherapy, formerly called hydropathy and also called **water cure**, [9] is a part of alternative medicine (particularly naturopathy), occupational therapy, and physiotherapy, that involves the use of water for treatment. The term encompasses a broad range of approaches and therapeutic methods that take advantage of the physical properties of water, such as temperature and pressure, for therapeutic purposes, to stimulate blood circulation and treat the symptoms of certain diseases [10]

We as dermatologists, can use water / hydrotherapy as a first line management or as an adjuvant therapy of xerosis and associated disorders to minimise the already burdened geriatric patients with their drug load.

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Spotter, What's your diagnosis ?

Dr Paschal Dsouza

Director Professor, Dermatology, ESIPGIMSR, New Delhi.

Answer:

Basal cell carcinoma (BCC)- nodular pigmented variant

- Basal cell carcinoma (BCC) is the most common form of skin cancer. Also known as rodent ulcer it is prevalent in elderly males. Classically seen over head and neck in areas prone to photodamage. Other risk factors include previous BCC or other form of skin cancers, skin phenotype which is fair with blue eyes and blond or red hair, previous cutaneous injury, thermal burn, chronic skin disease, inherited syndromes like basal cell naevus syndrome (Gorlin syndrome), Bazex-Dupré-Christol syndrome, Rombo syndrome and xeroderma pigmentosum

- Nodular pigmented variant of BCC is seen here as shiny pigmented nodule with a smooth surface, central ulceration, local tissue destruction & rolled edges. Other variants include superficial BCC, morphoeic BCC & basosquamous BCC. Biopsy from lesion is diagnostic



- Treatment depends on its type, size, location, number of lesions and the preference or expertise of the doctor. Most BCCs like one depicted here are treated surgically followed by flap or skin graft. Cryotherapy, photodynamic therapy, imiquimod & 5-fluorouracil can be used for superficial BCC. Long-term follow-up is desirable. Recurrent or metastatic BCC requires combination of treatments including surgery, radiotherapy & targeted therapy like vismodegib and sonidegib

Geriatric Quiz

Dr. N Asokan & Dr. T J Premjith

- 1) All features are suggestive of senile purpura, **EXCEPT**
 - a) Size of lesion <5cm
 - b) Lesions limited to the covered areas of the body
 - c) History of topical steroid use at the site can be a contributory factor
 - d) Irregular margins for the lesions

2. All are causality assessment tools for drug reaction **EXCEPT**
 - a) Naranjo algorithm
 - b) BARDI
 - c) RUCAM
 - d) STOPP/START

3. Which of the following is **NOT** a risk factor for developing vitamin D deficiency in elderly?
 - a) Female gender
 - b) Fair complexion
 - c) Reduced renal function
 - d) Obesity

4. Patient with history of multiple visits to different dermatologists presented with itching and crawling sensations of skin. Examination showed excoriations and erosions. Consider the following statements.
 - A) Matchbox sign/ specimen sign can suggest delusional parasitosis
 - B) Chronic pruritus screening is required
 - C) Schizophrenia should be considered
 - a) All are correct
 - b) b, c are correct
 - c) a, c are correct
 - d) a, b are correct

5. A patient who is recovering from recent cerebrovascular event, presented with macerations and erosions on the perineal area. Patient is otherwise healthy. Poor response to treatment with antifungals and cloxacillin. Most probable diagnosis would be
 - a) Candidiasis
 - b) Staphylococcal infection
 - c) Acrodermatitis enteropathica
 - d) Moisture associated dermatitis

6. Atrophic vaginitis may be caused by all **EXCEPT**
 - a) Reduced coital activity
 - b) Nulliparity
 - c) Cigarette smoking
 - d) Oral contraceptive use

7. All are true about Peyronie's disease **EXCEPT**

- a) Scar tissue deposition occurs in tunica albuginea
- b) TGF β 1 is important in pathogenesis
- c) More frequent in middle age than old age
- d) Pentoxifylline and vitamin E can have beneficial effect

8. An elderly female presented with recent onset hot flushes, tingling sensation, irritability, depression, insomnia, itchy dry vagina and urinary incontinence. She recently attained menopause. The drug most effective in the treatment of her vaso motor symptoms will be

- a) systemic estrogen
- b) medroxy progesterone acetate
- c) venlafaxine
- d) vitamin E

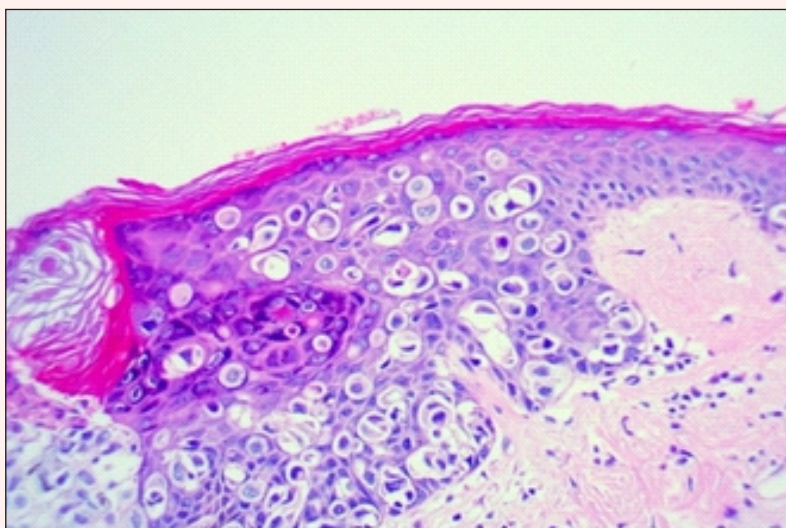
9. Elderly male presented with the following lesion of 5 year duration near nose which was of slow onset gradually enlarging initially small translucent and raised edges with recent central ulceration with no other systemic manifestations. Choose the correct statements among the following about the most likely diagnosis



- A) It is a premalignant lesion
- B) It is the second most common type of all skin cancers worldwide
- C) Retraction artefact is a characteristic finding in biopsy
- D) Photodynamic therapy is a useful option in some types

- a. A and B
- b. A and C
- c. A and D
- d. B and C
- e. B and D
- f. C and D

2. A 60 yr old woman presented with itching and burning on the vulva with a single pink coloured sharp margined lesion as shown below involving mucosa, slowly enlarging for more than one year, KOH smear was negative, no response to topical steroids. Histopathology picture is given. Which all statements are CORRECT?



- A) Adenocarcinoma is the most common underlying malignancy
- B) It occurs more commonly as a secondary lesion than as primary
- C) CEA serum level is useful in prognosis
- D) Recurrences are rare after wide excision

- a. A & B
- b. A & C
- c. A & D
- d. B & C
- e. B & D
- f. C & D

Geriatrics quiz answers

1. b

Bateman purpura usually occurs on sun exposed area as irregular macule,

2.d

It is for intervention in elderly to prevent unnecessary prescription , all others causality assessment

(O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2 [published correction appears in Age Ageing. 2018 May 1;47(3):489]. Age Ageing. 2015;44(2):213-218.)

3.b

(Meehan M, Penckofer S. The Role of Vitamin D in the Aging Adult. J Aging Gerontol. 2014;2(2):60-71.)

4. a.

(Rooks Text book of dermatology, UK 9th ed. 2016. P 86.1)

5. d

(Ladha M, Wagg A, Dytoc M. An Approach to Urinary Incontinence for Dermatologists. J Cutan Med Surg. 2017;21(1):15-22.)

6. d

Estrogen in OCP can prevent atrophic vaginitis

7. c

more prevalent in elderly (6 times)

(Ostrowski KA, Gannon JR, Walsh TJ. A review of the epidemiology and treatment of Peyronie's disease. Res Rep Urol. 2016;8:61-70.)

8.a

(Dalal PK, Agarwal M. Postmenopausal syndrome. Indian J Psychiatry. 2015;57(Suppl 2):S222-S232.)

9.f

Explanation: BCC is a malignant lesion; not a premalignant lesion; it is most common type (nearly 80 %) of all skin malignancies; retraction artefact help to differentiate from benign lesions like trichoepithelioma, and photodynamic therapy may be useful in superficial cases

10. b

Explanation: 25 % extra mammary Paget's disease has underlying adenocarcinoma, but primary disease is more common (up to 75% with no underlying malignancy). A high CEA serum level is a bad prognostic indicator, recurrences are common even with wide excision, and Mohs surgery is better choice.

CROSSWORD

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Z	M	O	X	I	B	U	S	T	I	O	N	C	E	E	J	U	A
A	T	S	A	U	Q	Z	H	N	A	I	E	S	B	U	Q	F	U
I	R	O	D	G	F	G	U	O	V	L	A	L	I	B	R	Y	E
T	I	L	D	B	Q	Z	G	L	I	E	P	B	I	N	Z	Q	I
P	F	W	R	D	U	B	T	Z	S	S	O	B	O	F	P	W	O
M	L	R	E	T	Q	O	K	A	M	U	L	B	E	R	R	Y	P
D	U	A	S	S	E	S	N	B	O	V	I	H	N	R	O	S	F
T	R	P	S	A	T	E	X	P	D	S	T	A	S	B	M	X	K
R	I	A	I	Z	G	E	M	S	E	O	A	O	I	S	O	P	N
Y	D	M	N	Q	R	G	E	G	G	E	N	A	S	E	N	S	E
O	I	A	A	D	R	R	I	H	I	X	H	Q	A	F	T	I	B
Q	N	D	D	M	E	E	G	N	B	S	J	Z	B	Y	O	D	R
H	E	L	D	D	M	M	W	O	O	P	W	O	R	R	R	V	W
S	H	T	R	I	F	L	U	R	I	D	I	N	E	C	Y	B	I
A	C	E	E	L	S	I	R	S	I	K	L	F	C	V	S	Q	O
N	Y	S	S	R	Q	N	Z	P	V	L	L	Z	U	I	G	T	P
B	P	E	S	G	Y	M	W	S	D	A	A	N	T	Q	U	R	C
R	L	E	I	G	H	Q	C	G	I	N	N	S	V	V	E	O	N
Y	U	L	N	O	F	L	U	H	O	E	S	C	H	W	C	J	L
X	F	E	S	P	R	E	M	Q	W	B	E	X	S	V	O	R	Z

CLUES:

Across

1. Practice of burning dried moxa placed in cone shaped piles over acupuncture points(11)- Row 1
4. Gene family encoding for proteins which mediate significant cellular effects of hedgehog signaling(3)- Row 4
6. A pattern of clustering of eruptive xanthomas in Fredrickson type IV lipoproteinemia(8)- Row 6
8. Antisense Bcl-2 oligonucleotide which targets Bcl-2 messenger RNA(9)-Row 10
12. An antiviral drug available only as topical used for acyclovir resistance cases(12)-Row 14
13. Syndrome with SURF1 mutation presenting as hypertrichosis(5)- Row 18
14. Procedure to detect excessive urinary porphobilinogen using Ehrlich's reagent(6)- Row 19

Down

2. Nails in elderly characterized by absent lunula , 3 horizontal bands of white, pink and opaque discolorations(10)- Column 12
3. A hedgehog signaling pathway inhibitor, SMO antagonist, used in BCC(10)- Column 10
5. A histopathological sign in Kaposi's sarcoma, where newly formed vessels project into pre-existing capillaries(10)- Column 16
7. Antagonist of bone morphogenic protein highly expressed in BCC stroma(7)- Column 7
9. Ulcers seen in metastatic Crohn's disease(8)- Column 14
10. Molecular marker of endothelium identified by antibody MECA 79 (10)- Column 4
11. Itch, generalized pruritus in elderly without any identifiable cause(7)- Column 12

Crossword Answers

1. Moxibustion
2. Neapolitan
3. Vismodegib
4. GLI
5. Promontory
6. Mulberry
7. Gremlin
8. Genasense
9. Sabrecut
10. Addressins
11. Willans
12. Trifluridine
13. Leigh
14. Hoesch

