Issue - 10

BIANUAL PUBLICATION OF THE BANGALORE DERMATOLOGY SOCIETY

IADVL: BDS BULLETIN

BANGALORE DERMATOLOGICAL SOCIETY SINCE 1998

2018

"DERMADRISHTI"

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A note from the presidential desk:

We are happy to continue with the BDS newsletter-"DERMADRISHTI", which covers all aspects of the activities of our Bangalore Dermatological society, a vibrant branch of the IADVL. This news letter is brought out bianual by the editorial team comprising of Dr. Leelavathy B. and Dr. Praveen Kumar S. I wish all the success to this academic activity and request all the members of BDS to contribute actively to the journal. This is an opportunity for young dermatologists and postgraduates to showcase their talent.

I wish Dr. Leelavathy B. and Dr. Praveen Kumar S. all the very best to take this journal to greater heights.

Dr. R. Raghunatha Reddy

President

Bangalore Dermatological Society

Presidential Message

It is with immense pleasure that I accepted the role of the President ship of Bangalore Dermatological society for the year 2017- 2019.

First of all let me thank, all my senior colleagues and all the members of the BDS for having trust in me to hold this prestigious post and also to host the academically mind boggling CME's, workshops, conferences, etc. I also thank all my colleagues and executive committee members for their support and encouragement.

To continue the good work of all my predecessors, I would like to enhance our goals.

Integrity

1. To enhance professional cohesiveness & to encourage the spirit of fraternity and the collegial spirit

Academics

3. To provide a platform for the upgradation of professional information, standards and skills
4. To guard and enhance professional and ethical standards of the members and thereby enhance the honor of the profession.

Digital

5. To make BDS completely paperless. All communication will be through mails, web site, messages, whatsapp and through other digital media.

Rural camps

6. To improve quality of life of people living in the rural areas through camps and awareness .

Memberships

7. The strength of any organization lies in the membership. So to see to it that every practicing dermatologist in Bangalore becomes a BDS member

CME's

8. To make every CME unique and worth the change.

Postgraduates

9. To encourage every PG student to participate , present cases and papers, compete, research and discuss and win laurels .

Unique programmes

11. To continue the tradition of introducing something unique in every term , eg. Capsules, Hand outs, Research grants etc .

Non dermatology talks

12. To introduce non dermatology talks for the benefit of all members, eg. investment, spirituality, fitness, etc to lead a better life

All this can be done only with the active participation, encouragement and support of all my team members, senior colleagues and the BDS fraternity .

I would like to thank all members for their continued co-operation and to help me make BDS successful, an important arm of IADVL.

Thank you and regards ,

Dr. R. Raghunatha Reddy

President

Bangalore Dermatological Society

Message from the Secretary

I congratulate Dr. Leelavathy B. and Dr. Praveen Kumar S.- on bringing out the BDS NEWSLETTER, highlighting the activities and achievements of BDS. This should serve as an inspiration for those involved with BDS activities and as a motivation for those contemplating to be a part of the same and bring the best out of them.

Long live BDS

Dr. Jagadish P.
BDS Secretary

Chief Editor's message

This year, Bangalore Dermatological Society brought the dermatologists of Bangalore closer, as a family, whilst sparing no effort in nurturing our knowledge of the subject.

The post graduates, the newer members of this organisation, have benefitted from the monthly meets, which were directed at strengthening our understanding of topics such as "Adverse drug reactions" and "Biologicals in the management of Psoriasis" to name a few. The quiz competitions, for the post graduates and the undergraduates managed to keep us on our toes as well.

The BDS team successfully organised the "Back to the ROOTS -2" conference in August 2017, which was attended by more than a thousand delegates from all over India. We also organised a family get together on 26th November at "Clarks exotica resort and spa" to recharge and renew ourselves while, providing an opportunity for us to connect and build stronger relationships with each other.

The BDS team's perseverance, and it's massive presence in IADVL-KN", has been rewarded with the honour of hosting Dermacon in 2019.

I invite contributions to our biannual BDS Bulletin "DERMADRISHTI", from one and all, including innovative ideas, original research and, of course, the occasional, but essential write up that is the perfect amalgam of humour and subject matter. It is the perfect platform for the junior residents to gain visibility and hone their writing skills. I, especially, encourage them to contribute to this magazine.

I would like to sincerely thank the President, the Secretary and EC of BDS, for giving me the opportunity of being the editor of DERMADRISHTI.

Dr. Leelavathy B.
Chief Editor
Bangalore Dermatological Society

Executive Editor's message

Bangalore Dermatological Society is a close knit group of vibrant dermatologists. The IADVL BDS bulletin "DERMADRISHTI" was a concept of Dr. P.M. Sangolli with whom I was associated and we have brought out 9 issues in the past.

This bulletin is a platform which unearths scientific and writing talents amongst dermatologists young and old.

I am happy to be of service as the executive editor to the best of my ability under the able guidance of our Chief Editor Dr. Leelavathi and past Editor Dr. Prabhakar M Sangolli.

We are happy in bringing out the 10th issue of our bulletin and we hope that with continued patronage of all of you we would be able to index the journal in the near future.

I thank our president Dr. Raghunath Reddy, Secretary Dr. Jagadish and all our exective committee members for helping me to serve our Bangalore Dermatological Society.

I wish that this bulletin will reach greater heights in future.

Dr. Praveen Kumar S MD, DNB, MNAMS
Executive Editor
Bangalore Dermatological Society

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Dr. Prabhakar M Sangolli, Senior Practising Dermatologist, Bangalore

Deleterious effects of environmental pollutants on skin:Needs urgent attention !!

Pollution is defined as contamination of the earth's environment with materials which interfere with human health, quality of life, or the natural functioning of the ecosystem. The major types of pollution are water pollution, air pollution, noise pollution and soil pollution. The WHO defines air pollution as contamination of the indoor or outdoor environment by any chemical, physical, or biological agent that modifies the natural characteristics of the atmosphere.Common sources are homes,vehicles,industries. Etc.Carbon monoxide,sulfur dioxide are the common particulate matter in the pollutants.Air pollution is the commonest cause for skin,lung disorders.

Skin is the first line of defense.UV radiation,polycyclic hydrocarbons,nitrogen dioxide,heavy metals,cigarette smoke damage skin barrier and induce various skin disorders. Pollution downregulates skin redox system resulting in free radical induced tissue damage and inflammation.It causes severe alteration of normal functioning of proteins,lipids and DNA of skin resulting in extrinsic skin ageing,triggering inflammatory and allergic disorders such as atopic dermatitis,contact dermatitis,acne,psoriasis etc..

Air quality guidelines take into account particulate matter,carbon monoxide,sulfur dioxide,nitrogen monoxide ,ground level ozone to determine air quality index. Ideal value is 50.Higher indices denote poor air quality

Ultraviolet radiation: Loss of stratospheric ozone by refrigerent gases,photochemical smog resulted in ultraviolet A.Ageing changes include solar elastosis,telangiectasia,pigment spots and coarse wrinkles.UVB also increase production of stratifin. Free radicals increase synthesis of AP-1 which downnregulates synthesis of collagen1 and 3.It also increase synthesis of matix metalloproteinases and NfKB increase production of inflammatory cytokines.
UVB causes immunosuppression which may increase the risk of BCC and SCC. Air pollutants disperse UVB, but UVA is unaffected

Smoking and skin

Skin has numerous deleterious effects on skin. It breaks down antioxidant defence system,reduces collagen synthesis and increases metalloproteinase synthesis

1. Smoker's face: Characterized by sallow skin with prominent maxilla, wrinkles and dyschromia
2. Induces comedonal acne
3. Worsens psoriasis
4. Enhances the risk of cutaneous malignancies
5. Induces mucosal pigmentation

Polyaromatic hydrocarbons

Main sources are vehicle emission and cigarette smoking. Other important source is waste incineration. By producing free radicals they result in premature aging, comedones,skin cancers and lymphoma. Chloracne can result in liver,kidney,nerve damage apart from acneiform eruptions

Ground level ozone

It is normally found in very low concentration .Ozone increase free radical formation in the epidermis resulting in premature aging. It also oxidizes squalene resulting in comedone formation.It also increases activity of dermal matrix metalloproteinase activity.

Particulate matter

Particulate are nanosized matters arising from factories, vehicle, construction sites. They enter thru' appendages and damage cell mitochondria.they also carry toxic metals. Poly aromatic hydrocarbons also damage DNA .They also worsen inflammatory dermatoses like atopic dermatitis.

Volatile organic compounds

The sources are paints, solvents, emission from vehicles. They worsen atopic dermatitis and other eczemas. They also result in appearance of precancerous conditions

Atmospheric oxides

Common ones are nitrogen dioxide,sulfur dioxide and carbon monoxide. They are responsible for generation of reactive oxygen species. Carbon monoxide contributes to increased incidence of flexural eczema.

Heavy metals
Cadmium,mercury and lead are the common ones. Sources are cement,vehicle fumes

Prevention strategies:
Control of air pollution at work places,schools

Well ventilated work places,air filters, improved manufacturing practices
Environmental pollution can be minimized by less sulfur in vehicle fuel,using CNG,car pools etc.

Personal protection with protective clothing,masks and barrier creams with anti oxidants are some of the measure which can be practiced to minimize the deleterious effects of air pollution

Skin is the largest organ of human body, and any factor affecting skin health will impact the body as a whole. Major air pollutants having deleterious effects on the skin include UV rays, polycyclic aromatic hydrocarbons, volatile organic compounds, various oxides, particulate matter, ozone and cigarette smoke. Sunlight, smoking and particulate matter have a role to play in extrinsic skin aging. Smoking has also been associated with skin cancer, psoriasis, acne . Exposure to surface ozone has been associated with urticaria, eczema, contact dermatitis etc. Polyaromatic hydrocarbons cause extrinsic skin aging, pigmentation and acneiform eruptions. Oxides have been associated with increased prevalence, as well as worsening of atopic dermatitis in children.

Reference:
Puri P, Nandar SK, Kathuria S, Ramesh V. Effects of air pollution on the skin: A review. Indian J Dermatol Venereol Leprol [serial online] 2017 [cited 2017 Sep 23];83:415-23

Approach to Genodermatoses

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Abstract

Genodermatoses are a group of inherited disorders involving both cutaneous and systemic signs and symptoms. In the past few years' diagnosis of genetic skin diseases is not restricted to clinical examination and diagnosis, but has come long way in confirming the diagnosis by genetic testing and also providing genetic counselling. Recent advances in genetic counselling have found their way into clinical dermatology. Approximately one-third of all hereditary disorders show cutaneous finding and in most of the cases it provides a clue to diagnose the disorder. This article reviews the step-wise approach to evaluate patients with genodermatoses.

Key words: genodermatoses, genetic analysis, genetic counselling, prenatal diagnosis

Introduction

Diagnosis of genetic skin disorders is a challenging task, even in the hands of experienced geneticist and dermatologist. Skin acts as a mirror for underlying systemic disorders with approximately one-third of all the hereditary disorders showing characteristic cutaneous features. [1] The dilemmas in diagnosing genetic disorders are due to rarity of the condition, lack of awareness, their diversity, overlapping or heterogeneous phenotypes, complicated nomenclature and classification, development of newer technology and dearth of data in developing countries due to lack of publishing and research in the speciality. In the past few years there are approximately 350 classic genodermatoses that has been mapped to specific loci and linked to specific gene defects. [2] All genetic disorders with their features have been listed in OMIM data base (Online Mendelian Inheritance in Man).

Approach to genodermatoses

Classification of genodermatoses is given in Table 1. A step wise approach is depicted in Table 2. [3]

Table 1: Classification of Genodermatoses

1.	**Inherited immunobullous disorders**
	Epidermolysis bullosa of different groups
2.	**Disorders of keratinization**
	Ichthyosis
	Palmoplantar keratoderma
	Erythrokeratoderma
	Follicular keratoses
3.	**Hereditary disorders of pigmentation**
	Carney complex
	Chediak–Higashi syndrome
	Griscelli syndrome
4.	**Familial multiple tumor syndromes**
	Neurofibromatosis types 1 and 2
	Tuberous sclerosis complex
	Gardner syndrome, Cowden syndrome
	Peutz–Jeghers syndrome
5.	**Ectodermal dysplasias and disorders of ectodermal appendages**
6.	**Disorders with defects in DNA-repair and chromosomal instability**
	Bloom syndrome
	Xeroderma pigmentosum
	Cockayne syndrome
7.	**Poikilodermatous disorders**
	Rothmund–Thomson syndrome
	Dyskeratosis congenita
	Acrokeratotic poikiloderma of Weary
	Kindler syndrome
8.	**Connective tissue disorders**
	Ehlers–Danlos syndrome
	Pseudoxanthoma elasticum
	Marfan syndrome

Table 2: Stepwise approach to case of genodermatoses

Step1: Complete history with pedigree chart
Step 2: Complete examination (cutaneous and extracutaneous)
Step 3: Recognizing red flags of genodermatoses
Step 4: Provisional diagnosis
Step 5: Laboratory testing
Step 6: Genetic testing
Step 7: Genotype phenotype co-relation
Step 8: Genetic Counselling- Prenatal and pre implantation genetic studies

Step 1: Complete history with Pedigree chart

Thorough history includes country of origin (culture traditions), age of onset, age at diagnosis, consanguinity, family history of genetic disorders, family pedigree, antenatal history, previous pregnancy details (miscarriages, still birth), birth history (preterm birth, type of delivery), sibling history, presentation of skin at birth (collodion membrane, blisters, erythroderma) and development history. Parents may be reluctant to give information of the family history, but explaining about the importance of family history in diagnosing can help to gather correct information. Repeated questioning may help in identifying newly discovered or forgotten information. In a child with suspected incontinentia pigmenti asking history of presence of similar lesions at birth or presence of subtle linear hypopigmented streaks on the body will help to counsel family about the mode of inheritance and prognosis.

Family history is very important to establish the mode of inheritance (autosomal dominant/autosomal recessive/X-linked or mitochondrial disorders) especially in our country where there is lot of consanguineous marriages. A three generation family history (also called as 'first genetic test') in the form of pedigree is the gold standard for establishing the mode of inheritance. [4]

Step 2: Complete Examination

Thorough cutaneous examination including hair, nails, teeth, genital and oral mucosa is important. Identification of particular skin and appendageal changes can narrow the differential diagnosis and can

sometimes come to a final diagnosis also. Some of the cutaneous markers that can help in diagnosing underlying genetic disorders are listed in [Table 3]. Presence of woolly hair, total absence of hair, hypotrichosis, and silvery grey hair with other association can diagnose underlying genotrichosis [Table 3]. [5] Nail and teeth abnormalities can be present in ectodermal dysplasia and epidermolysis bullosa. Oral leukotrichia is involved in dyskeratosis congenita

A look for extracutaneous manifestation is important as some of the genodermatoses have grave prognosis. References to other specialist are necessary to rule out extracutaneous symptoms. Silvery hair syndromes can present with immunodeficiency. Cardiomyopathy is a feature of Carvajal and Nexos syndrome. [6] Early diagnosis of these symptoms can help to prevent complications. Cardiac rhabdomyomas are amongst the earliest and most specific manifestation of tuberous sclerosis and these tumours are detected prenatally. Ichthyosis with keratitis and deafness present as KID syndrome.

Step 3: Recognizing red flags of genodermatoses

Some of the cutaneous features like collodion membrane, erythroderma, loose skin, blister at birth, silvery hair can give a clue to diagnose underlying genetic disorders. [7,8] Recognizing these red flags of dermatology is at most important to narrow down our diagnosis Table 4.

Table 3: Some of the red flags for diagnosing genodermatoses

Red flag/cutaneous mrkers	**Genetic Disorder**
Collodion baby	Autosomal recessive ichthyosis (Non bullous ichthyosiform erythroderma, lamellar ichthyosis), Syndromic ichthyosis
Neonatal erythroderma	Netherton syndrome, autosomal recessive ichthyosis,
Blisters at trauma sites	Epidermolysis bullosa
Resistant eczema with recurrent infections	Immunodeficiency disorders (Hyper IgE syndrome)
Photosensitivity	DNA repair disorders (cockyane syndrome, Rothmund-Thompson syndrome, kindler syndrome)
Lax skin	Cutis laxa, Ehlers-danlos syndrome
Silvery grey hair	Griscelli syndrome, chiediak-higashi syndrome, Elajalde syndrome
Multiple Cafe-au-lait macules	Neurofibromatosis, tuberous sclerosis

Step 4: Provisional diagnosis

Based on the clinical features a provisional diagnosis can be considered. This can be corroborated by further laboratory and genetic testing which will aid in confirming the diagnosis.

Step 5: Laboratory testing

Skin biopsy for histopathological examination, special stain, and immunohistochemistry may help diagnosis of genetic skin disorders and detect malignancy as a complication as in case of xeroderma pigmentosum. Histopathology can help to distinguish keratinocyte and sebaceous nevi, multiple trichoepitheliomas which can provide a clue for Brooke-Spiegler syndrome. Skin biopsy for antigen mapping in epidermolysis bullosa helps to delineate the subtype of epidermolysis bullosa which helps in genetic counselling and prognosis. Biochemical and enzymatic test are important tools for diagnosis metabolic and nutritional disorders. X-linked recessive ichthyosis can be confirmed by low steroid sulfatase activity. Light microscopy can aid to diagnoses hair shaft disorders like silvery grey hair syndromes, trichorrhexis nodosa, trichorrhexis invaginata and pili torti. Presence of trichorrhexis invaginata can give a clue to diagnose netherton syndrome, pili torti in menke kinky hair syndrome. [9] Polarized microscopy can aid in diagnosing trichothiodystrophy which shows alternate light and dark bands (tiger tail appearance).

Step 6: Genetic testing

Though many genetic skin disorders can be diagnosed clinically with laboratory testing, confirmation of the disorder by doing genetic analysis helps to predict the outcome, severity by genotype and phenotype correlation, risk of recurrence in the subsequent pregnancies and patient management.

- Molecular testing is helpful to predict asymptomatic family members at risk of developing the condition and also family members
- In symptomatic family members who might be carriers of a recessive disorder
- In patients with unclear phenotypes
- For prenatal and preimplantation genetic studies

Genetic testing may not be mandatory in cases where there is well defined phenotypes, and in patients not planning to have children where it is not benefited. 5ml of blood should be obtained in an EDTA tube and subjected to DNA extraction and further genetic testing. Recently NGS (Next generation sequencing) has revolutionised genomic research. An entire human genome can be sequenced within a single day and this captures a broader spectrum of mutations than Sanger sequencing. [10]This will allow clinicians to take genetic information to the bedside. The online databases which provide up to date information on genodermatoses are GeneReview, Orphanet, OMIM, Pubmed, ADF Genetik.

Step 7: Genotype-phenotype correlation

Genotype-phenotype correlation helps in confirming the final diagnosis and the novel mutations associated with complex phenotypes. Genodermatoses like Xeroderma pigmnetosum, Cockyane syndrome, and Trichothiodystrophy show mutations in one single gene with distinct diseases thus exhibiting clinical heterogeneity. Genetic heterogeneity refers to identical clinical phenotypes caused by mutations in different genes as in autosomal recessive congenital ichthyosis. Genotype-phenotype correlation helps in counselling, better prognosis, development of pathogenesis-based disease classifications and targeted therapies. [10]

Inconclusive cases can be followed up regularly; DNA can be preserved along with detailed clinical features. New clinical features may develop with age and point to the diagnosis and the gene responsible may be found.

Step 8: Genetic counselling

Mutational analysis offers appropriate genetic counselling to parents and makes DNA-based prenatal diagnosis and preimplantation genetic studies feasible in high risk families. Prenatal diagnosis should be offered to couples with only fatal genetic disorders. There are only few centres in our country offering preimplantation genetic studies.

Current scenario in our country

- Due to the better understanding of genetic basis of genodermatoses and tremendous progress in molecular diagnosis, few dermatologists are carrying out genetic testing as a part of the research for fatal genetic skin disorders which helps in genetic counselling.
- Though there is no dearth of data in our country, there is definitely lack of facility for genetic testing at an affordable price for common man and one has to bank on private genetic laboratories with high pricing.
- Another pertinent issue is lack of national registries in India unlike in western countries for genetic skin disorders which may help in future to formulate guidelines for management
- Multicentric studies with multi-speciality involvement are necessary for genetic skin disorders which are not at present feasible in our country.
- Dermatologists should take up research studies in the field of genodermatoses to understand the magnitude of the problem as well as genotypes (mutation) specific to Indian population.

References

- Irvine AD, McLean WHI. The molecular genetics of the genodermatoses: progress to date and future directions. Br J Dermatol 2003;148:1-13.
- Itin PH, Burger B. Genodermatosen in der täglichen Praxis – die Rolle des Dermatologen Therapeutische Umschau 2010;67:483-5.
- Tantcheva-Poór I. , Oji V, Has C. A multistep approach to the diagnosis of rare genodermatoses. J Dtsch Dermatol Ges. 2016;14:969-986.
- Gutmacher A, Collins FS, Carmona RH. The family history- more important than ever.N Engl J Med 2004;351:2333-6.
- Sinclair R, de Berker D. Hereditary and congenital alopecia and hypotrichosis. In: Dawber RP, editor. Disease of the Hair and Scalp. 3rd edn. Oxford: Blackwell Science; 1997. pp. 252–397.
- Srinivas SM, Kumar P, Basavaraja G. Carvajal Syndrome. Int J Trichol 2016;8:53-55.
- Aradhya SS, Srinivas SM, Hiremagalore R, Shanmukappa AG. Clinical outcome of collodion baby: A retrospective review. Indian J Dermatol Venereol Leprol 2013;79:553
- Sahana MS, Sacchidanand S, Hiremagalore R, Asha GS. Silvery grey hair: clue to diagnose immunodeficiency. Int J Trichol 2012;4:83-5.
- Aradhya SS, Srinivas SM, Hiremagalore R, Shanmukappa AG. Netherton syndrome masquerading as psoriatic erythroderma. Indian J Paediatr Dermatol 2014;15:89-91
- Kwon E, Basel D, Siegel D, et al. A review of next generation genetic testing for the dermatologist. Pediatric Dermatol 2013;30:401-8.

Old wine in new bottles – revisiting neglected dermatologic therapies
Part I – Topical agents

Dr. A.L. ShyamPrasad, Professor of dermatology, Ramaiah Medical college.

In the history of dermatologic therapy, there has been a varied and esoteric range of agents used. Some have been derided, some taken up enthusiastically, some have fallen in favour with the advent of newer and more effective and/ or commercially profitable products. Of the last group, there has been a revival of sorts for some medications. In this short review, some of the topical agents which are again finding favour for various reasons are revisited. Part I will look at topical agents.

Gentian violet

Gentian violet ((GV) hexamethyl pararosaniline, (also known as crystal violet, methyl violet) is a triphenylmethane dye with anti-bacterial, anti-fungal, anti-helminithic, anti-trypanosomal, anti-angiogenic and anti-tumor properties, and has been used in a wide variety of skin conditions. [1] The use of GV in pyodermas and candidiasis is very old, but due to it's cosmetically unappealing quality, it was being supplanted by other agents. However, it's effectiveness against Gram positive organisms and especially Methicillin resistant Staph aureus [2], has led to a revival in interest, especially for limited infections, and prevention of colonization of prosthetic valves and in nasal carriers of MRSA. Gendine, a combination of GV and Chlorhexidine has been used successfully for sterilizing urinary catheters3,due to it's effectiveness against Gram negative organisms and Candida. GV has been used in treatment of candidial oral infections in HIV patients. Of particular interest has been the discovery of its effect on blockage of NADPH oxidase, which results in anti-angiogenic activity, which could result in discovery of new uses, as angiogenesis is implicated in a variety of disorders including skin tumours and viral infections.

Crude Coal Tar

A product derived during the destructive distillation of wood or charcoal, coal tar has been used in dermatologic disorders for a long time. It is believed to be a complex organic compound with as many as 10,000 organic chemicals in it. Consequently, attempts to refine it have met with limited success,

probably because the effect has been due to the combined action of all these compounds, known as the pleiotropic effect. Liquor picis carbonis, used for decades in dermatology settings, has been shown to be quite effective in an evidence based review.[4] Coal tar and salicylic acid combinations, especially in palmoplantar psoriasis, and in combination with sunlight or broad band UVB therapy, probably leads to longer remissions than calcipotriol or calcipotriol with steroids, although long term studies on this are lacking. In the University of California,San Francisco, a modified Goeckerman's regimen consisting of application of coal tar followed by UVB , has shown a reduction to PASI-75 by 3 months, with a long term remission of 9.5 months to a year, which is superior to even the latest biologic agents .[5] Admittedly, the therapy is tedious and time consuming, but the relative freedom from side-effects and the long remission periods make it worthwhile for moderate to severe psoriasis.

Sodium thiosulphate lotion

Sodium thisosulphate 20 to 25% solution was used in earlier days as a standard treatment of Pityriasis versicolor. It was also known as “hypo” and was a reagent in developing photo films. With the advent of digital cameras, this gradually became difficult to procure and the broad spectrum topical antifungal agents ensured that it was hardly being used. However there have been a couple of case reports [6,7] which have used a 10% lotion in calcinosis cutis. They have reported disappearance of the deposits within 5 -6 months of application.

Whitfield's ointment

A combination of benzoic acid with salicylic acid, in varying percentages, has been used for dermatophyte infections ever since it was formulated in 1907 by Arthur Whitfield. While studies, in general, on most topical antifungal preparations are of low quality, an earlier study comparing Clotrimazole with Whitfield's ointment showed comparable efficacy[8], while another showed that it was comparable to Butenafine[9]. With the present epidemic of resistant superficial fungal infections sweeping India, one would expect that this cheap and effective medication would again become popular. It's only drawback is potential irritation, and it should be used with caution in flexural areas.

Tolnaftate

This cheap and effective topical agent against dermatophytoses gradually became unavailable in India with the advent of the commercially more lucrative broad spectrum antifungals. In an in-vitro study, it's efficacy against dermatophytes has been found to be better than Itraconazole, terbinafine, fluconazole, griseofulvin, butenafine,econazole and miconazole[10]. As with Whitfield's ointment, this should again start becoming popular with increasing fungal resistance to the azoles.

References

1 Maley AM, Arbiser JL.Gentian Violet: A 19th century drug re-emerges in the 21st century. Exp Dermatol. 2013 December ; 22(12): 775–780. doi:10.1111/exd.12257Berrios RL, Arbiser JL.

2 Effectiveness of gentian violet and similar products commonly used to treat pyodermas. Dermatol Clin. 2011; 29:69–73.

3 Hachem R, Reitzel R, Borne A, et al. Novel antiseptic urinary catheters for prevention of urinary tract infections: correlation of in vivo and in vitro test results. Antimicrob Agents Chemother. 2009; 53:5145–5149

4 Slutsky JB, Clark RA, Remedios AA, Klein PA.An evidence-based review of the efficacy of coal tar preparations in the treatment of psoriasis and atopic dermatitis. J Drugs Dermatol. 2010;9(10):1258–1264.

5 Serrao, R. & Davis, M.D. Goeckerman treatment for remission of psoriasis refractory to biologic therapy. Journal of the American Academy of Dermatology. 2009: 60, 348-349

6 García-García , López-López , Álvarez-Del-Vayo , Bernabeu-Wittel J. Iatrogenic calcinosis cutis successfully treated with topical sodium thiosulfate. Pediatr dermatol. 2017 May;34(3):356-358.

7 Jost J , Bahans C , Courbebaisse M et al. Topical Sodium Thiosulfate: A Treatment for Calcifications in Hyperphosphatemic Familial Tumoral Calcinosis? J Clin Endocrinol Metab. 2016 Jul;101(7):2810-5.

8 Gooskens V, Pönnighaus JM, Clayton Y, Mkandawire P, Sterne JA.Treatment of superficial mycoses in the tropics: Whitfield's ointment versus clotrimazole. Int J Dermatol. 1994 Oct;33(10):738-42

9 Thaker SJ, Mehta DS, Shah HA, Dave JN, Kikani KM. A comparative study to evaluate efficacy, safety and cost-effectiveness between Whitfield's ointment + oral fluconazole versus topical 1% butenafine in tinea infections of skin. Indian J Pharmacol. 2013 Nov-Dec;45(6):622-4.

10 Baghi N, Shokohi T, Badali H et al. In vitro activity of new azoles luliconazole and lanoconazole compared with ten other antifungal drugs against clinical dermatophyte isolates. Med Mycol. 2016 Oct 1;54(7):757-63.

CASE REPORT WITH QUIZ

Dr. Leelavathy, Professor and HOD BMCRI, Bangalore

22 year old male patient presented with asymptomatic nodular lesion over the face (near left infra-orbital area) since 9 months and has suddenly increased in size since 2 weeks(Fig 1). Initially the lesion was size of a grain and has suddenly increased to the present size in a span of 2 weeks. On examination Well defined solitary, superficial, soft, non tender nodular lesion measuring 1x 0.5 cm lesion present over medial aspect of left infra-orbirtal rim. Blood Investigation(CBC including Platelet count, BT, CT, RBS , HIV, HbsAg, HCV, VDRL & systemic examination) were within normal limits. Lesion was Excised and sent for Histopathological examination.

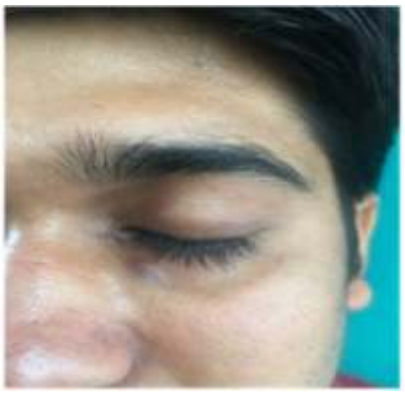


Fig 1

Histopathological Section (Fig 2) showed tumor lobules separated by band of collagen, lobules are composed of mixture of congested capillaries surrounded by fascicles of bland spindle shaped endothelial cells and pericytes. Slit-like vascular spaces were seen. Focal area with epitheloid cells containing friable cytoplasm were seen.

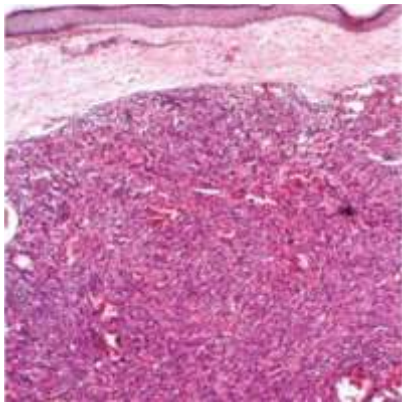
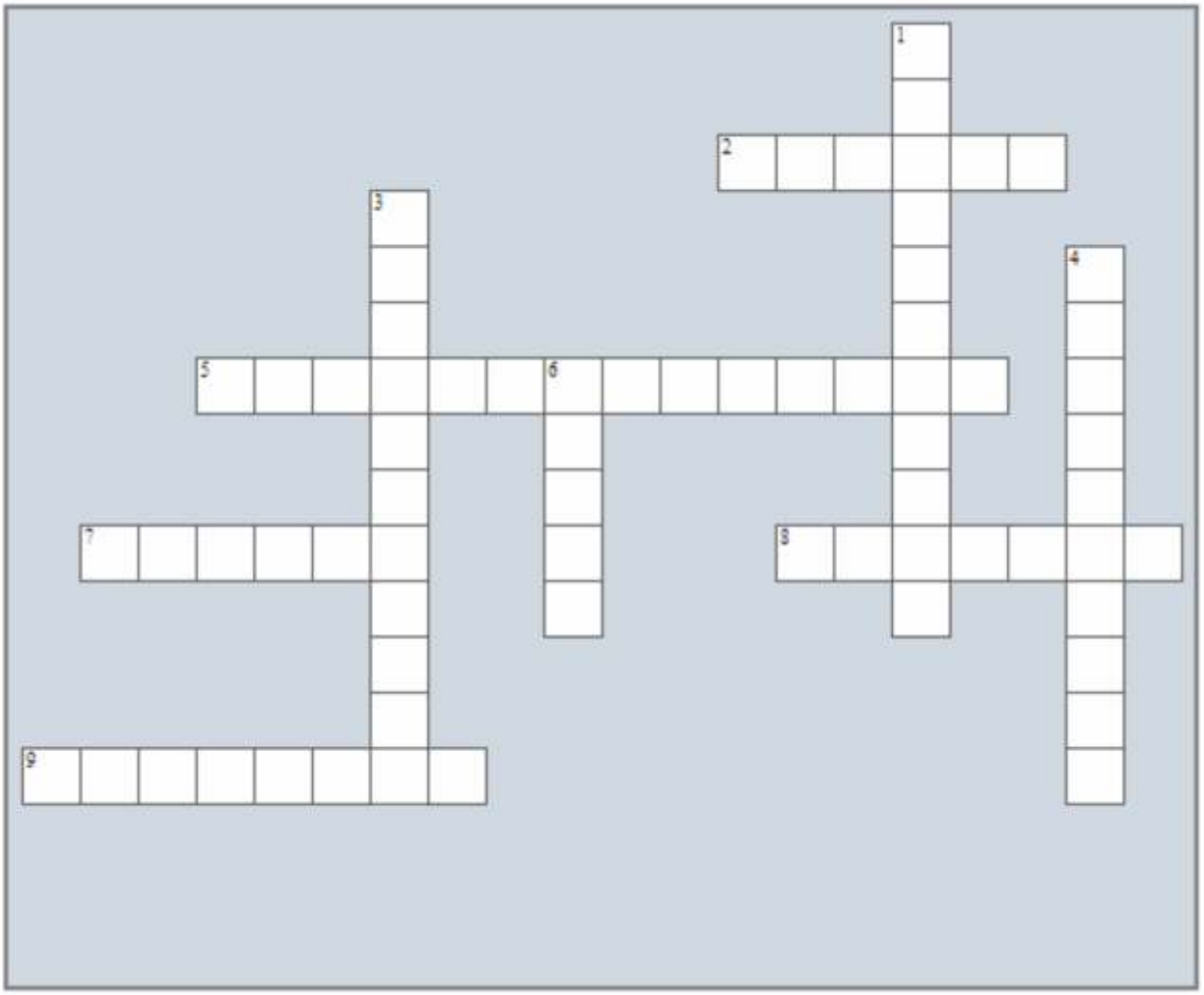


Fig-2

What is your Diagnosis ?

Cross Word Puzzle

Dr. K.N. Shivaswamy, Associate Professor of dermatology, Ramaiah Medical College.



Across

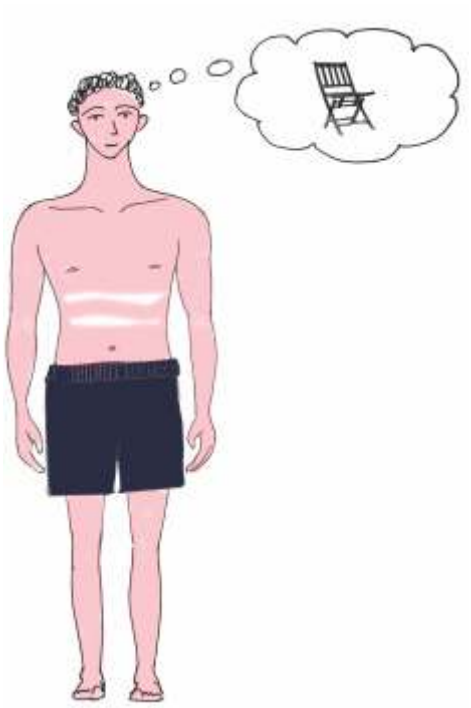
2. Wind blown appearance on histology (5)
5. Seborrhoeic keratosis following subsidance of Erythroderma/Eczema (6,8)
7. Histological appearance in cylindroma (3,3)
8. Painful interdigital neuroma (7)
9. Cells seen in Hibernoma (8)

Down

1. Lymphocytic collection in Stratum corneum in PLC (6,5)
3. This pink stain on eyelids and forehead, stains blood vessels of brain too (11)
4. Histological appearance in Tufted angioma (6,4)
6. This itchy condition burns with flame (5)

Dermacartoons

Dr. Prarthana, Juior Resident of dermatology, Ramaiah Medical College.



Answer to Case Report with Quiz

Diagnosis- KaposiformHaemangiendothelioma

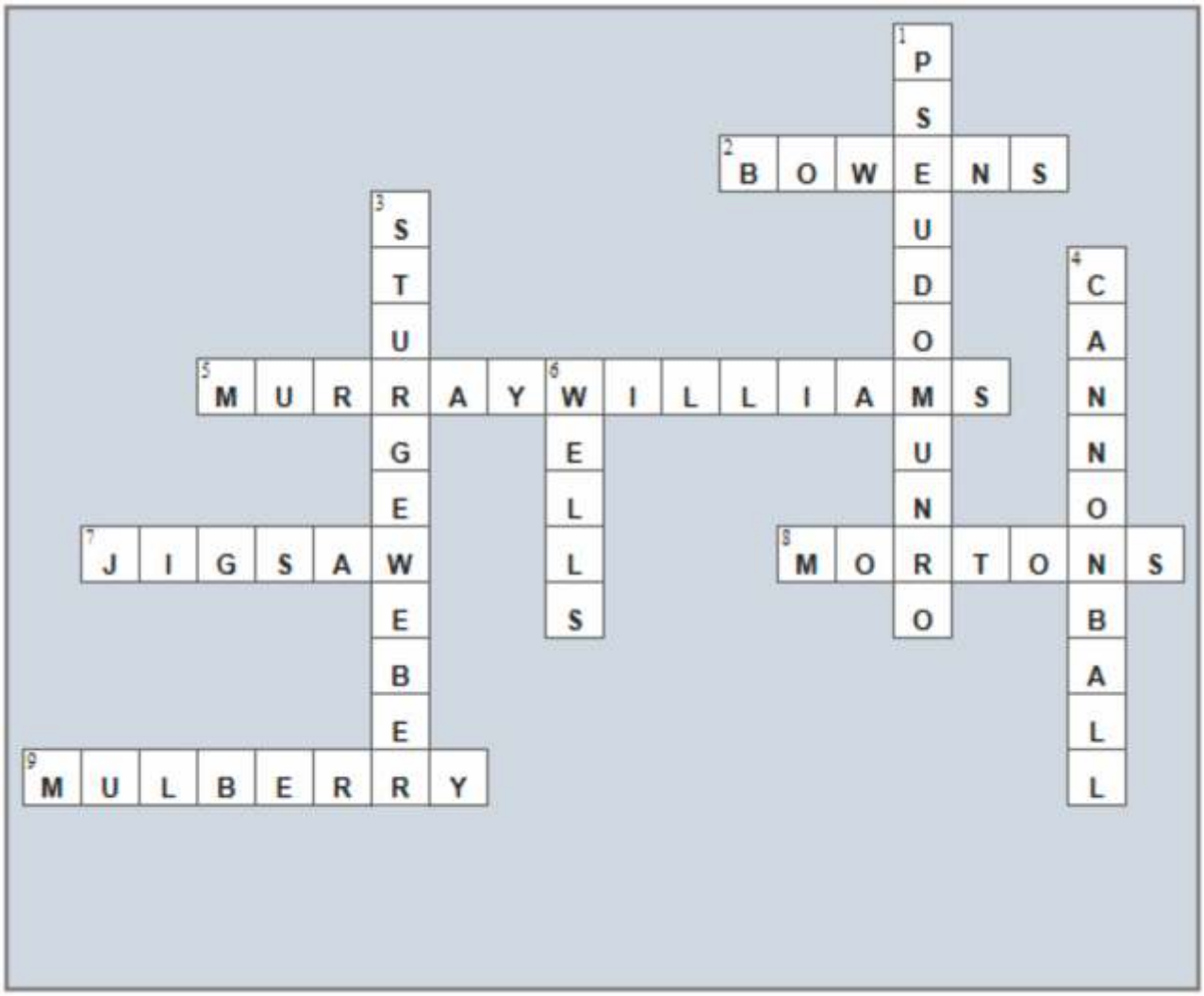
- Kaposiform hemangioendothelioma is a rare locally aggressive vascular tumor of the skin, deep soft tissue and bone in children. Characterized by infiltrating nodules and sheets of spindle cells, and resemblance to Kaposi's sarcoma. Long-term biologic behavior of this tumor remains undetermined. The term "kaposiform" relates to its unmistakable resemblance to Kaposi's sarcoma. "Hemangioendothelioma" implies the uncer- tainty regarding the biologic behavior of such tumor, situated somewhere between hemangioma and angiosarcoma. KH may be locally very extensive and aggressive, but has not shown any metastatic potential, though death has resulted from severe coagulopathy. Only about 18% of reported patients demonstrated retroperitoneal tumor, while a third of the patients showed involvement of the trunk or the limbs, and cutaneous lesions were observed in nearly 75% of the reported cases. Cutaneous appearance of KH is generally not distinctive, apart from the extensive "port wine" hemangiomatous presentation.

- The diagnosis rests on the histology, and on its correlation with clinical features. Histopathology shows Lobules with infiltrative growth pattern. Lobules composed of congested capillaries surrounded by spindle shaped endothelial cells and pericytes.Slit-like vascular space are characteristic. Complications include Kasabach – merritt phenomenon, a profound Thrombocytopenia resulting from platelet trapping within tumour & recurrence. Treatment include Complete Excision , If large /deep seated- Embolization, Chemotherapy (Vincristine, propranolol) & Low dose Radiotherapy

References:

1. Beaubien ER, Ball NJ, Storwick GS. Kaposiform hemangioen- dothelioma: a locally aggressive vascular tumor. J Am Acad Dermatol 1998;38:799 – 80
2. Mentzel T, Mazzoleni G, Dei Tos AP, Fletcher CDM. Kaposi- form hemangioendothelioma in adults. Clinicopathologic and immunohistochemical analysis of three cases. Am J Clin Pathol 1997;108:450 –5.
3. Fukunaga M, Ushigome S, Ishikawa E. Kaposiform haeman- gioendothelioma associated with Kasabach-Merritt syn- drome. Histopathology 1996;28:281–4

Answer to Crossword Puzzle



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Answer to Dermacartoons

Hertoghe's sign (Queen Anne's sign)

It is defined as loss of lateral one third of eye-brows (superciliary madarosis). It is seen in leprosy, myxedema, hypothyroidism, follicular mucinosis, atopic dermatitis, trichotillomania, ectodermal dysplasia, discoid lupus erythematosus, alopecia areata, syphilis, ulerythema ophryogenes, systemic sclerosis and HIV infection.

Deck-chair sign

It was classically described in Papulo-erythroderma of Ofuji, wherein there is flat-topped red papules that become generalized erythrodermic plaques without the involvement of abdominal skin folds.

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