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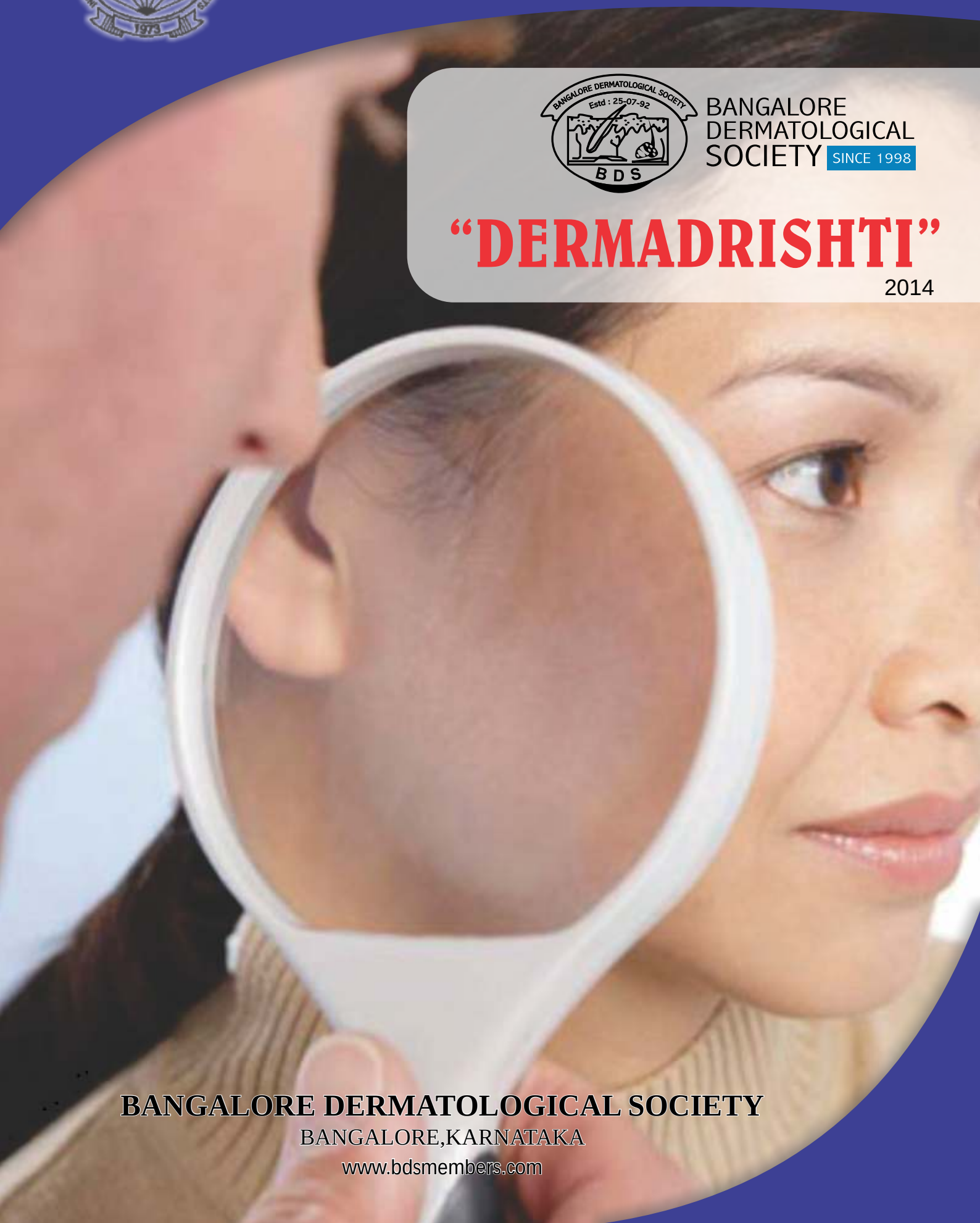

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INDEX

CONTENTS:

Antiretroviral therapy at glance

K. Hanumanthayya – Professor
Jaidev Yadav – Assistant professor
G. Balasubrahmanyam – Assistant professor
Dr Safia Tanyeem – PG Students
Dr Jaya Pathak – PG Students
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ART reduces HIV replication. Body viral load is reduced. Opportunistic infections are reduced. Cost of management is reduced. Patients can lead a productive life.

ART has changed HIV/AIDS from a virtualdeath sentence to a chronic manageable disease.

Steps in HIV Replication and the drugs acting at different stages –

HIV Virus

⇐ CCR5 Receptor antagonists – Maraviroc and Vicriviroc

⇓

Attachment to CD4+T Lymphocytes

⇐ Fusion Inhibitors – Enfuvirtide

⇓

Fusion and Uncoating

⇐ NRTIs, NNRTIs

⇓

Reverse transcription

⇐ Integrase Inhibitors – Raltegravir and Elvitegravir

⇓

Integration

⇓

Transcription and Translation

⇓

Virus assembly

⇐ Protease Inhibitors

⇓

Budding and Maturation

⇓

Release

Anti Retro Viral Drugs –

In 1986 US FDA approved Zidovudine to treat HIV/AIDS patients – Monotherapy.

In 1995 US FDA approved second drug Didanosine – Dual therapy.

In 1996 US FDA approved Protease inhibitors and recommended triple therapy.

In 2010 US FDA approved 26 ART drugs.

In 2014 US FDA approved 37 ART drugs.

Classification of ARDS –

Nucleoside Reverse Transcriptase Inhibitors

Drug	Analog of	Dose
Zidovudine (Azidothymidine)	Thymidine	300 mg bid
Stavudine	Thymidine	20-30 mg bid
Zalcitabine	Cytidine	0.75 mg tid
Lamivudine	Cytidine	150 mg bid
Emtricitabine	Cytidine	200 mg od
Didanosine	Adenine	150-200 mg bid
Abacavir	Guanosine	300 mg bid

Nucleotide Reverse Transcriptase Inhibitors

Tenofovir disoproxil fumarate	Adenosine	300 mg.

Mechanism of action

NRTIs enter the CD4 cells and are converted to their corresponding triphosphate derivatives, which have a high affinity for HIV reverse transcriptase enzyme, which is required for DNA synthesis. The NRTIs are nucleoside analogues.

They competitively inhibit reverse transcriptase, are incorporated into viral DNA chain and terminate DNA chain elongation.

Tenofovir is a nucleotide analogue and competitively inhibits HIV reverse transcriptase similar to nucleoside analogues.

Non nucleoside Reverse Transcriptase inhibitors –

Nevirapine 200 mg od X 14 days. Induction dose.

200 mg bid, maintenance dose.

Delavirdine 400 mg tid.

Efavirenz 600 mg at bedtime.

Etravirine 200 mg bid.

Rilpivirine 25 mg od.

Mechanism of action – The NNRTIs bind to reverse transcriptase enzyme and inactivate the enzyme. Hence viral RNA will not get converted into viral DNA.

NNRTIs are effective only on HIV-1.

Protease Inhibitors –

Saquinavir / Ritonavir.	Saq/r	1000/100mg bd.
		1600/200mg bd.
Indinavir / Ritonavir.	Idv/r	800/100mg bd.
Lopinavir / Ritonavir	lpv/r	400/100mg bd.

553/133mg bid when combined with EFV or NVP

Nelfinavir	nfv	1250mg bd.
Atazanavir	atv	400mg bd.
Atazanavir / Ritonavir.		300/100mg bd.
Amprenavir		1200mg bd.

Mechanism of action –

The protease inhibitors bind competitively to HIV protease and block viral maturation. This makes the daughter viral particles immature and noninfectious. It is needed for the production of mature virion and for viral infectivity.

Entry Inhibitors –

a) Fusion Inhibitor –It binds to a glycoprotein of the virus and inhibits the binding of the virus to the host cell membrane, and thereby blocks the entry of the virus into the cell, hence called fusion inhibitor, thus prevents transmission of HIV. Enfuvirtide 90 mg is given subcutaneously twice daily.

b) CCR5 Receptor Antagonists – CCR5 is a coreceptor involved in fusion and entry of the virus into the CD4 cells. Maraviroc and Vicriviroc selectively bind to CCR5 receptors and block the entry of HIV into the cells. Maraviroc 300 mg bid and Vicriviroc 30 mg OD.

Integrase Inhibitors – Raltegravir and Elvitegravir bind to integrase and prevent integration of HIV-DNA into the chromosome of the host cell.

Treatments of HIV infection – Currently several drugs are available for the treatment of HIV infection and with appropriate medication it is possible to control the disease and prolong life expectancy . Combination of drugs like HAART regimen is used to improve efficacy and delay the development of resistance. WHO recommends fixed dose combination to improve compliance. Zidovudine or tenofovir combined with lamivudine or emtricitabine form the first

line drugs. If first line therapy fails, second line drugs are given.

WHO 2010 Guidelines –

When to start: All adolescents and adults including pregnant women with HIV infection and CD4 counts of < 350 cells/mm3, should start ART, regardless of the presence or absence of clinical symptoms. Those with advanced clinical disease should start ART irrespective of their CD4 cell count.

What to use in first line therapy: First line therapy should consist of an NNRTI + two NRTIs, one of which should be zidovudine or tenofovir.

Three drugs are given.

Zidovudine or Tenofovir

+

Lamivudine

+

Nevirapine or Efavirenz

What to use in second line therapy: Second line ART should consist of ritonavir boosted protease inhibitor plus two NRTIs, one of which should be zidovudine or tenofovir.

Tenofovir or zidovudine

+

Didanosine

+

Lopinavir/r or Atazanavir/r

Occupational Post Exposure Prophylaxis –

In health care workers exposed accidentally, ART should be initiated as soon as possible within first 4 hours. Not later than 72 hours.

Basic Regimen – AZT 300 mg + Lamivudine 150 mg twice daily for four weeks.

Expanded Regimen – AZT 300 mg + Lamivudine 150 mg + Lopinavir or Ritonavir 200 mg twice daily for four weeks.

References –

1) Koda, Kimble & Young's Applied Therapeutics, The Clinical Use of Drugs. 10th edition, 2013.
2) Medical Pharmacology, 4th edition, 2013. Padmaja Udaykumar.
3) B B Rewari, Delhi, Medicine Update 2010.
4) National Guidelines on Second line ART for Adults and Adolescents – NACO April 2011.

BACTERIAL INFECTIONS – AN UPDATE

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Skin and Soft tissue infections, now called as acute bacterial skin and skin structure infections (ABSSSIs) are a common group of infections indicating infections in skin and its structure derivatives.

It accounts for about ? 10% of hospital admissions in the USA. Various geographic studies have shown that methicillin resistant staphylococcus aureus – hospital acquired MRSA (HA) accounts for 12-76% of patients in hospitals and methicillin resistant staphylococcus aureus community acquired MRSA (CA) - up to 30% of cases. In the evolved setting of day care centers where patients get into the hospital in the day and return in the evening the overlap between HA and CA is getting mixed and a new terminology called Health care associated infections is used which is defined as infections in community based patients who have had contact with the health care system and thus may have been exposed to potentially resistant pathogens.

Resistance to methicillin is provided by the mecA gene encoded within the staphylococcal cassette chromosome mec (SCCmec), which has been horizontally transferred multiple independent times from related staphylococcal species into methicillin-susceptible precursor strains. To date, five primary SCCmec types have been identified with differing gene content and organization. Prior to the 1980s, MRSA was primarily associated with healthcare facilities and carried SCCmec types I, II, or III. The emerging CA-MRSA strains have acquired SCCmec types IV or V, which distinguish them from earlier HA-MRSA strains.

The important differences between MRSA (CA) and MRSA (HA) are listed below in the table:

	CA – MRSA	HA - MRSA
Clinical spectrum	Via SSTI	Via RT, UTI, blood stream
epidemiology	Clusters and outbreaks in closed population	Healthcare associated
Underlying condition	Dermatological	Hospital acquired infection
Age group	Younger	older
Toxin production	More	fewer
Resistance pattern	Susceptible to multiple antibiotics	Resistant to antibiotics
Genotype	SccMec IV	SccMev I, II, III
Virulence	PVL present	PVL absent

Classification: SSTIs have been classified depending on various factors:

1. Etiological agent
2. Layer of involvement – skin, subcutaneous tissue, fascia, muscle etc.
3. Acute and chronic.
4. Localized or generalised.
5. Necrotizing and non – necrotizing.
6. Primary and secondary (associated with pre-existing skin diseases)
7. Infectious diseases society of America (IDSA) classification is as follows

   Superficial

   Uncomplicated – Impetigo, erysipelas

   Ncrotizing infections

   Infections associated with bites and animals

   Surgical site infections

   Infections in the Immuno compromised host
8. ERON et al

• Class I SSTI but no systemic toxicity or no co-morbidity

• Class II Systemically well but with co morbidity or systemically unwell.

• Class III Toxic and unwell

• Class IV Sepsis syndrome and life threatening infection.

10 An SSTI is said to be uncomplicated when it presents with superficial bacterial infections such as: Impetigo, erysipelas, folliculitis, furunculosis, and superficial cellulitis.

An SSTI is said to be complicated if it presents with the following features:

Involvement of deep tissues including subcutaneous fat.

Need for surgical intervention.

Involvement of the perianal area.

Infection of the foot in a diabetic patient.

Presence of significant coexisting diseases

75 cm of redness, edema or induration

DIAGNOSIS: can be made by 5 different approaches.

1. MICROSCOPY: this carries low sensitivity and specificity; inability to isolate organisms for detection
2. CULTURE: may require special media; some are uncultivable; potential health risk; low yield and expensive.
3. SEROLOGY – Detection of antibodies. Results vary
4. DETECTION OF MICROBIAL ANTIGENS AND PRODUCTS
5. MOLECULAR TECHNOLOGY – Identify Nucleic acids Using DNA Probes. the various tests are Polymerase Chain Reaction (PCR), Ligase Chain Reaction (LCR), Transcription Mediated Amplification (TMA), Nucleic Acid Sequence-based Amplification (NASBA)

They carry the advantage of being Highly Accurate in Diagnosis; even in conditions when it is Difficult To Culture Or Ascertain Through Standard Histologic methods and more importantly can be Used To Identify

Antimicrobial Resistance

As per the new recommendations—Blood cultures should be obtained & biopsy with culture considered if patient presents with

- Malignancy
- Severe systemic S/S's (high fever/hypotension)
- Unusual predisposing factors
- Immersion injuries, animal bites, Neutropenia and severe Cell-mediated immunodeficiency.

The following Lab features are used to recognize complications in a case of SSTI.

- White blood cell count.
- C- reactive protein levels.
- Hb%
- S – Sodium
- S – Creatinine.
- Glucose levels

Wong et al have used these scores and have recommended that <5/13 – indicates low risk of complication; >6/13 indicates higher risk of complications. When used clinically they have a High sensitivity and specificity of >95%.

In addition to CRP, Serum procalcitonin levels have been found to be a reliable marker for bacterial infection. They are more sensitive and specific than CRP. Their levels are elevated much earlier than other clinical or lab features like fever, changes in white blood cell count and blood cultures.

Treatment: antibiotics form the mainstay of management in cases of SSTI. Numerous antibiotics have been discovered. Their usage is limited by various factors and thus a search for an ideal antibiotic is still continuing.

An ideal antibacterial should exhibit the following characteristics:

- Selective target
- Bactericidal
- Narrow spectrum
- High therapeutic index
- Few adverse reactions
- Various routes of administration.
- Good absorption.
- Good distribution to site of Infection.
- Emergence of resistance is slow.

The search for an ideal antibiotic has still eluded. Virtually all antibiotics discovered have ended up having developed resistance within a few years after its introduction.

Making the condition more worrisome is the fact that research towards discovery of newer antibiotics are dwindling. In the last five years only one antibiotic has been discovered which has already exhibit resistance.

Thus if we don't take steps to prevent the misuse of antibiotics we will be left with virtually no agents to fight against these infections.

Health workers recommend the use of antibiotics rationally, which is defined as "Rational use of drugs requires thatpatients receive medications appropriately to their clinical needs, in doses that meet their own individual requirements for anadequate period of time, at the lowest cost to them and their community"

To overcome the above discussed issues, a good antibiotic policy depending on the microbial activity in the particular geography needs to be framed at every hospital. Such an antibiotic policy will help improve patient care by promoting the best practice in antibiotic prophylaxis and therapy; retard the emergence and spread of multiple antibiotic resistant bacteria; provides guidelines for appropriate therapy; eliminates the use of unnecessary or ineffective antibiotics and restrict the use of expensive or unnecessarily powerful ones.

This will help the hospital have own list of therapeutic antibiotics as first- line antibiotics; reserved agents; restricted agents and withdrawn agents etc.

The following guidelines have been recommended for good practice of ANTIMICROBIAL PRESCRIBING:

1. Send for the appropriate investigations in all infections as recommended for diagnosis, prognosis and follow up of these infections.
2. Differentiation between contamination, colonization and infection is important to choose a right antibiotic.
3. Choice of antibiotics: This depends on antibiotic susceptibility of the causative Organism. Toxicity, Efficacy, Rapidity of action, Pharmacokinetics and Cost. Use the most effective, least toxic and least expensive antibiotic for the precise duration of time needed to cure or prevent infection.
4. Clinical Diagnosis: Some antibiotics are specific for the disease and thus can be easily selected. However some conditions like deep cellulitis etc may have difficulty in establishing the etiological agent and thus may lead to difficulty in choosing an appropriate antibiotic. In such instances one should seek a bacteriological diagnosis.
5. Empiric Therapy – If the causative agent is not known and where delay in initiating therapy would be life threatening or risk serious morbidity, empiric antimicrobial therapy based on a clinically defined infection is justified.
6. The need for antimicrobial therapy should be reviewed on a daily basis. For most Infections 5 – 7 days of antimicrobial therapy is sufficient.
7. All IV antibiotics may only be given for 48 – 72 hours. After this consideration of oral alternatives, based on clinical or laboratory outcome is recommended.
8. Some guiding principles for escalation:
   (a) If ESBL +ve:
   (b) For confirmed MRSA infections and not MSSA.

(c) In case of Pan drug resistant Pseudomonas /Acinetobacter sp infection

9. Treatment with antibiotic combinations: The use of antibiotic combination is desirable under the following situations:

(a) During the investigation of an obscure illness

(b) In long term therapy e.g. treatment of tuberculosis.

(c) To achieve synergistic effect, e.g. in treating infective endocarditis.

(d) Mixed infection, when one drug is not effective against the pathogen.

(e) To permit a reduction of the dose of potentially toxic drug.

The following combinations are synergistic

i. Aminoglycoside and β–lactam antibiotic.

ii. β–lactam antibiotic and β–lactamase inhibitor.

iii. β–lactam antibiotic and cell wall inhibitor (Vancomycin)

iv. Sulphamethoxazole and Trimethoprim.

6. Antimicrobial drug therapy cannot be considered in isolation and other aspects of therapy must be taken into account in judging the effect of treatment. Some of them are incision and drainage, correction of septic shock, hypoxia, anemia etc, and surgical removal of obstruction.

III. RESERVE ANTIMICROBIALS

Some antimicrobials are held in reserve to maintain their effectiveness in treating certain difficult infections by reducing the spread of microbial resistance. Some of them are: Carbapenems and Linezolid, Colistin, Aminoglycosides etc.

The following criteria has been proposed to protect them from overuse –

1. Severe sepsis as defined by more than one organ failure.
2. Clinical failure of other classes of antibiotics over 48 hours in terms of worsening inflammatory markers, unresolving fever and new/worsening hemodynamic instability.
3. The organism is susceptible to only such specific drugs as per culture report.

A list of the newer generation antibacterials is given in the table below

SSTI - NEWER ANTIBIOTICS

IV. HYPERSENSITIVITY

All patients should be asked about drug allergies and drug intolerance. This is the responsibility of the treating physician. He then has to document in drug chart as

No known allergy (NKA).

History not available.

Advances in topical therapies:

S. aureus is a ubiquitous Gram-positive bacteria and a commensal organism of humans, colonizing the anterior nares of approximately 32% of the population. Administration of systemic antibiotics to decolonise the nares has been proved to be ineffective.

Perioperative Mupirocin for 5 days reduces MRSA infection in orthopaedic/ vascular surgeries. A study has shown that screening for MRSA in those patients followed by decolonisation with Mupirocin and adequate barrier precautions during hospitalisation reduces MRSA infection three fold and thereby reduces the average length of stay in the hospital. Mupirocin has been the topical antibiotic of choice in the last two decades. Recently newer topicals have been discovered.

Of these retapamulin has also been proven to be effective in MRSA infections. Indolmycin has also shown efficacy but resistance has emerged. An isomer of nadifloxacin has been fourd to be effective against MRSA. This has led some workers to opine limiting its role in acne therapy. Rifampicin derivatives like rifalazil has also been proven effective but the threat of resistance and cross resistance has limited its use in SSTIs.

Research has focussed on searching for alternatives for topical antibiotics:

They include white petrolatum. Chlorhexidine, triclosan, and Dakin's solution.

Certain agents used in the earlier days like honey and sugar, eucalyptus oil. Oil from Bursera fruits and tea tree oil have been found to be effective in Mupirocin resistant MRSA stain.

In persistent carriers or patients with recurrent SSTIs, clinicians are advised to address the issue of "GAPS IN CARE". That is to

Address colonization in Groin, Axillae, Perianal, Skin folds.

Address the issue of Isolation.

Address the issue of Nares.

Address the risk factors for colonization in Cuts, Abrasions, Rooms and Eczematous skin.

To conclude, the prevalence of SSTIs are increasing. Staph aureus and streptococci are still the common pathogens though depending on the source of infection the responsible microorganisms vary. The number of antibiotics efficacious against these organisms are dwindling and antibiotic resistance is a major problem. Framing of antibiotic policy should emable us to use antibiotics more judiciously. Also the issue of topical therapies and alternate modes of therapy should help reduce the use of systemic antibiotics indiscriminately.

A Review of dermatoses of pregnancy

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Introduction

Many skin changes occur in pregnancy due to various alterations in hormonal, immunological and physiological factors that occur throughout pregnancy. Cutaneous changes in pregnancy can be classified into three groups- physiological changes, skin conditions improved or worsened by pregnancy and lastly the skin conditions that are specific to pregnancy termed 'pregnancy dermatoses' Some cutaneous alterations like melsma and erythema are physiological,

Some dermatoses are altered (improved or worsened) by pregnancy. Psoriasis is known to improve during pregnancy. 'Impetigo Herpetiformis' , a severe form of generalized pustular psoriasis occurs during pregnancy, usually in the third trimester. Varying in severity, it responds well to systemic prednisolone and usually subsides after delivery while some cutaneous alterations are specific to pregnancy. . Systemic Lupus Erythematosis worsens during pregnancy with increased risk of eclampsia and flare of lupus nephritis in the mother.

Finally, a group of disorders that occur during pregnancy are very specific to pregnancy and are termed 'pregnancy dermatoses' or 'dermatoses of pregnancy'. Classification of dermaoses of pregnancy has been difficult due to unclear and complex pathogenesis involved. The most recent classification by Ambros-Rdolph et al incudes four groups-pemphigoid gestationis, polymorphic eruption of pregnancy, intrahepatic cholestasis of pregnancy and atopic eruption of pregnancy. Atopic eruption is further sbclassified to include eczema of pregnancy, prurigo of pregnancy and pruritic folliculitis of pregnancy.

Before moving into detailed discussionon on pregnancy dermatosis, a brief look into the immunological changes in pregnancy offers some help in understanding them better.

Since mother and fetus are genetically dissimilar, it is arguable that normally mother's immune system should reject the fetus straight away. Immnological alterations so occur in the maternal system that the fetus is in fact rather protected from otherwise immunological rejection. T cell mediated immunity undergoes a change with the resultant shift in Th1 to Th2 ratio towards predominant Th2 response which includes secretion of cytokines IL-14 and IL-10 which are protective to fetus. Th1 response is blunted and the Th1 cytokines IL-12 and Interferon –gamma are reduced.

Polymorphic eruption of pregnancy (pruritic urticarial papules and plaques of pregnancy), (PUPP)

It is the most common of the pregnancy dermatoses. Typically it appears in third trimester; more common in primigravida. It is relatively benign and does not lead to any complications either to the mother or to the child.

As the name indicates, it presents with itchy urticarial papules, that later coalesce to form plaques, in the abdomen sparing the periumbilical region. Rashes typically appear in striae. In mild forms, rashes are restricted to abdomen; in severe forms rashes extend proximally to limbs. Eventually, target-like lesions or vesicles may appear. Pruritus is always severe. The rash usually subsides by 4-6 weeks. Histopathology reveals
Direct and indirect immunofluorescence studies are negative. Pathogenesis remains unknown.

Treatment involves educating the patient about the benign nature of the disease along with the use of antihstamines, topical steroids and in some severe cases judicial use of short course of systemic steroids would suffice.

Pemphigoid gestationis

Pemphigoid gestationis is the auto-immune condition specifically associated with pregnancy. Autoantibodies are directed against the non-collagenous(NC) extracellular (16A) domain of the hemidesmosomal glycoprotein BP 180(collagen xvii). BP 180 has intercellular, extracellular and transcellular components and is distributed in the basement membrane of skin and epithelium of umbilical cord and placenta. During pregnancy, antibodies that are directed against the placental antigen are formed and cross react with the antigen present in skin and umbilical cord. Although, maternal immune system would have developed tolerance to fetal tissue, abnormal antigen presentation by maternal HLA molecules could trigger the immune response against the NC 16A antigen. Antigen antibody reaction leads to activation of complement cascade, recruitment of inflammatory cells leading to disruption of basement membrane with accumulation of inflammatory cells and exudate. Direct Immunofluorescence studies show deposition of IgG4 subclass of IgG antibodies and C3 in a linear form along the BMZ (basement membrane zone). Of late, ELISA technique has been employed as a diagnostic lab test for diagnosing PG, due to its cost-effectiveness and ease of procedure. Elisa also has the advantage of giving antibody titres, as this mazy be useful in monitoring the disease activity and response to treatment. Immunoblotting is another more specific but an expensive test for detecting antibodies against NC16A antigen.

Incidence of pemphigoid getationis is approximately one in 50000 pregnancies. This autoimmune condition was earlier named as 'herpes gestationis 'due to presence of lesions resembling herpetiform lesions. PG is associated with other autoimmune disorders and

patients with PG express HLA-DR3 and HLA-DR4 molecules. Clinically it presents with pruritic urticarial and annular plaques in the abdomen and subsequently spreading to extremeties. Initial presentation mimics PUPP of pregnancy. This is initial phase followed appearance of vesicles and bullae. Pruritus is invariably present. Blisters are tense and do not easily rupture and later either show hemorrhagic crusting or get resorbed.

Investigations include skin biopsy and immunoflourescence studies. Monitoring the fetal well being is also of prime importance since PG is known to affect the fetus fetus. Mild disease responds to topical steroids and oral antihistamines. Severe cases require systemic steroids, dose being titrated against severity of the disease. Once disease is stable, Steroids should be tapered and maintained at sufficient dosage until delivery so as to prevent rebound of the disease. Disease remits after the child birth but in some patients, disease continues to be active for some length of time. Recurrences in subsequent pregnancies are a common. Uncontrolled disease poses danger to fetus; prematurity and small for dates fetuses are a common feature. Fetal morbidity and mortality are high in case of early onset of disease during pregnancy and uncontrolled disease.

Intrahepatic cholestasis of pregnancy

This is another rare disorder that occurs during the third trimester of pregnancy and resolves spontaneously after delivery. It presents with severe pruritus without any skun lesions. The exact pathogenesis of cholestasis is not clearly understood. It is more common in South American countries and south East Asia. Genetically predisposed individuals are more at risk. How environmental factors influence this disorder is not known. Mutations in any of the genes ABCB4, ATP8B1 and ABCB 11 pose the pregnant women to higher risk of developing cholestasis. These genes code for biliary proteins. Of these mutations, one involving the gene ABCB4 is most commonly studied. It codes for MDR3(multidrug-resistant-protein 3) p-glycoprotein. MDR3 P-glycoprotein transports lipids across the hepatocyte canalicular membrane and any mutations in ABCB4 will give rise to abnormal MDR3 p-glycoprotein that can not transport phospholipids resulting in cholestasis.

Clinically patients present with severe pruritus without primary skin lesions. Excoriations, erosions and crusting occurs secondary to scratching. Pruritus is severe at night. Abnormal liver functions invariably accompany pruritus except in a very early stage. Early identification of the disorder is important because of its adverse effects on fetus. Condition subsides after delivery but is known to recur in subsequent pregnancies. Icreased bile acid levels is the consistent finding, sometimes accompanied by increased bilirubin levels, altered liver enzyme

levels and dyslipidemia.

ICP can have serious consequences on child like preterm labor, fetal distress and fetal death depending on the severity of the disease. Bile acids are toxic to the fetus and cause placental hypoxia. Bile acids and their metabolites-deoxycholic acid and lithocholic acid
are directly toxic to fetus and cause fetal growth retardation and death.

Mainstay of treatment is aimed at reducing blood levels of bile acids in the mother. Ursedeoxycholic acid, a naturally occurring bile acid has been used successfully in decreasing the blood bile acid levels. Mechanism of action, though not completely understood, involves improved canalicular transport, decreasing the synthesis and secretion of endogenous bile acids, and protecting the hepatocytes from toxic effects of bile acids. Cholestyramine , dexamethasone and S-adenosyl 4-methinone have also been tried varying amount of success.

Atopic eruption of pregnancy

This last entity includes atopic eczema of pregnancy, prurigo of pregnancy and pruritic follicultis of pregnancy. Atopic eczema of pregnancy presents with pruritic papular eruptions or eczematous lesions on the background of dry skin. Immunological shift from Th1 to Th2 predominance during pregnancy probably acts as a trigger for atopic eczema of pregnancy in women with atopic background.. It presents in the first trimester. It runs a relatively benign course without causing any harmful effects on fetus or mother. Treatment is on the similar lines of management of atopic dermatitis.

Prurigo of pregnancy presents with pruritic excoriated papules and nodules on the extensor aspects of arms, legs and abdomen. Pruritic folliculitis presents with itchy follicular papules and pustules on back, chest, arms and abdomen. These conditions are benign and management is similar to atopic eczema.

Conclusion

Dermatoses of pregnancy are a group of skin disorders that are specific to pregnancy; some are benign while others are known to cause harmful effects on fetus and mother. Differentiating the harmful ones from benign conditions is essential since early initiation of treatment would decrease morbidity and mortality of both fetus and mother. Better understanding of the pathogenesis of these conditions could lead to more efficient snad safer pharmacotherapies.

Fever with rash

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Fever with rash is one of the common conditions encountered in the dermatology out-patient department. The differential diagnosis of fever with rash is extensive and a meticulous approach with a thorough history and clinical examination is needed to narrow down to a diagnosis. Here we will be discussing in brief about the approach to a case of fever with rash.

History:

History of exposure to any ill contacts at home or work place, pets or insects should be asked. Drug intake and immunization prior to the onset of the rash can give a clue to the etiology of rash. Travel history to any endemic area is very important in this era of globalization.

Temporal association of the rash with fever gives a clue to the diagnosis. Rash can appear before the onset of fever, simultaneously or after a latent period. The progression and evolution of rash like cephalo – caudal or centripetal distribution gives a clue to the diagnosis in certain viral exanthems like measles and varicella. Associated symptoms like itching or pain should be asked and also the location and distribution of rash.

Classification:

The rash can be classified based on their morphology or etiology. Morphologic classification of rash includes:

- Maculopapular
- Petechial
- Diffusely erythematous with desquamation.
- Vesiculobullous/pustular .
- Nodular

Etiologic classification:

- Viruses
- Bacteria
- Spirochetes
- Rickettsiae
- Medications
- Immune mediated disorders

Morphology	Condition
Macular/maculopapular rash	Measles, Rubella, Dengue, drug rash, Infectious mononucleosis, Chikungunya, Adenovirus/Enterovirus infection, Brucellosis, Rickettsial infection, Systemic lupus erythematosus
Vesicular	Varicella, Herpes simplex infection, enteroviral infection, SJS
Diffuse erythema/ scarlatiniform rash with desquamation	Scarlet fever, SJS, Drug induced TEN,Toxic Shock Syndrome, Kawasaki Disease
Urticarial	Infectious mononucleosis, Coxsackie, Yersinia, Borrelia
Petechial/purpuric	Dengue, chikungunya, Rickettsial Meningococcemia, Yersinia, Borrellia Bartonella, HSP, cut vasculitis

Fever	
Acute onset	Measles, Rubella, Erythema infectiosum, Varicella , Adenoviral infection, Coxsackie, Infectious mononucleosis, Scarlet fever, Toxic shock syndrome, Meningococcemia, Kawasaki disease
Insidious onset	Systemic lupus erythematosus, Poly arteritis nodosa,Wegener's granulomatosis
Relapsing	Borrelia, bartonella

Associated features	
Prodrome of URTI	Measles, Rubella, Erythema infectiosum, Varicella, Adenovirus infection, coxsackie, Ebstein Barr virus infection, Scarlet fever
Polyarthritis Small joints	Chickungunya, Dengue, leptospira infection
Large joints	Acute rheumatic fever Henoch Schonlein purpura (HSP)
Hepatosplenomegaly & lymphadenopathy	Infectious mononucleosis, Leptospirosis, Borellia, Brucellosis
Haemorrhagic	Dengue, Chikungunya, Meningococcemia

Difference between viral exanthem and drug rash

	Viral	**Drug**
History	prodrome	Drug intake
Fever	Mod-high	mild
Pruritus	Less/ -	more
Morphology	pinkish	More red
	progression	Sudden onset
		Palms& soles +
	Specific pattern	-
Clustering of cases		+
Lympadenopathy	+	DRESS
Arthralgia	+	-
Facial oedema		+
Blood count	lymphocytosis	Eosinophilia
complications	>	
Drug withdrawal & challenge		Prompt recovery Recurrence

Examination:

A detailed examination is necessary in all cases of fever with rash and one should look for

- The patient's vital signs and general appearance
- Signs of toxicity
- Adenopathy
- Oral, genital or conjunctival lesions
- Hepatosplenomegaly
- Evidence of excoriations or tenderness
- Signs of neck rigidity or neurologic dysfunction

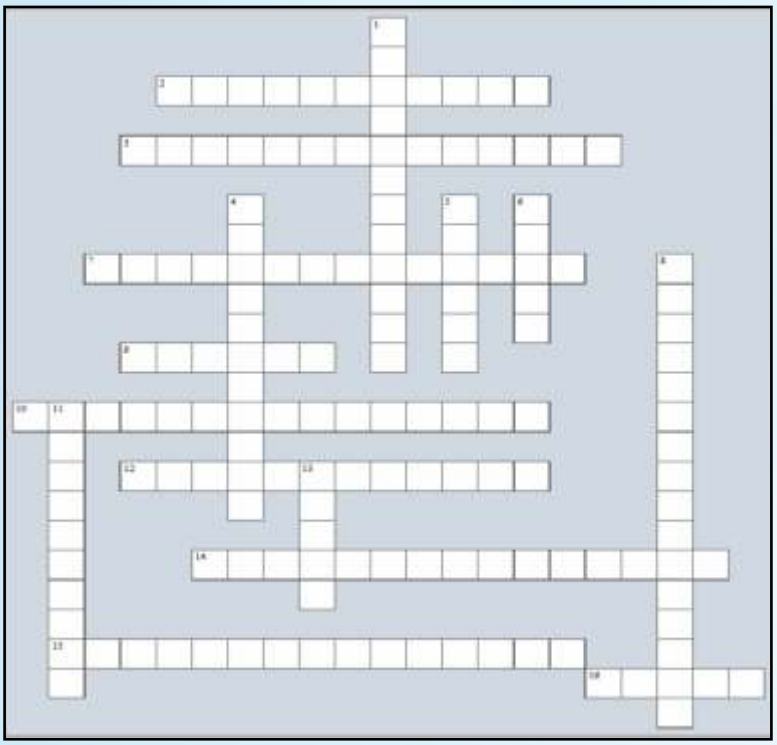
Non – specific viral exanthema:

Non specific viral exanthema is the most common type or exanthem seen in children. The rashes lack any characteristic features and usually shows blanchable erythematous macules/ papules. It is seen most commonly over the trunk and extremities and is not usually associated with itching. Most of the times the rash resolves within a week's time.

Here we have tried to give a general approach for the evaluation of fever with rash. Fever with rash can be benign as in case of non specific viral rash or can be associated with serious complications as in case of Kawasaki disease. Hence a care approach to any case of fever with rash is very important to arrive at a diagnosis.

5. CROSSWORD ON SIGNS

BY **DR. K.N. SHIVA SWAMY,** MS RAMAIAH HOSPITALS, BANGALORE



Across

2. Encephlofacial angiomatosis (6,5)
3. Papular acrodermatitis of childhood (8,6)
7. Pityriasis lichenoides et varioliform acuta (5,9)
9. Exudative discoid and lichenoid dermatitis of Sulzberger-Garbe (3,3)
10. Histiocytic necrotizing lymphadenitis (7,8)
12. Cutis hyperelastca (6,6)
14. Hereditary hemorrhgic telangiectasia (5,5,5)
15. Anaphylactoid purpura (6,9)
16. Hyperkeratosis follicularis et parafollicularis in cutem penetrans (5)

Down

1. Reticular pigmented anomaly of flexures (7,5)
4. Aplasia cutis with limb reduction anomaly (5,6)
5. Angiolymphoid hyperplasia with eosinophilia (6)
6. Mal del pinto (5)
8. Dermatofibrosis lenticularis disseminata (7,9)
11. Congenital onychodysplasia of index finger (3,7)
13. Acute febrile neutrphilic dermatoses (5)

(Answers to Crossword on Page No.19)

4. Case report with Quiz

Dr. Shubhani Saini -Postgraduate**, Dr. Praveen Kumar. S** - Assistant Professor**,**
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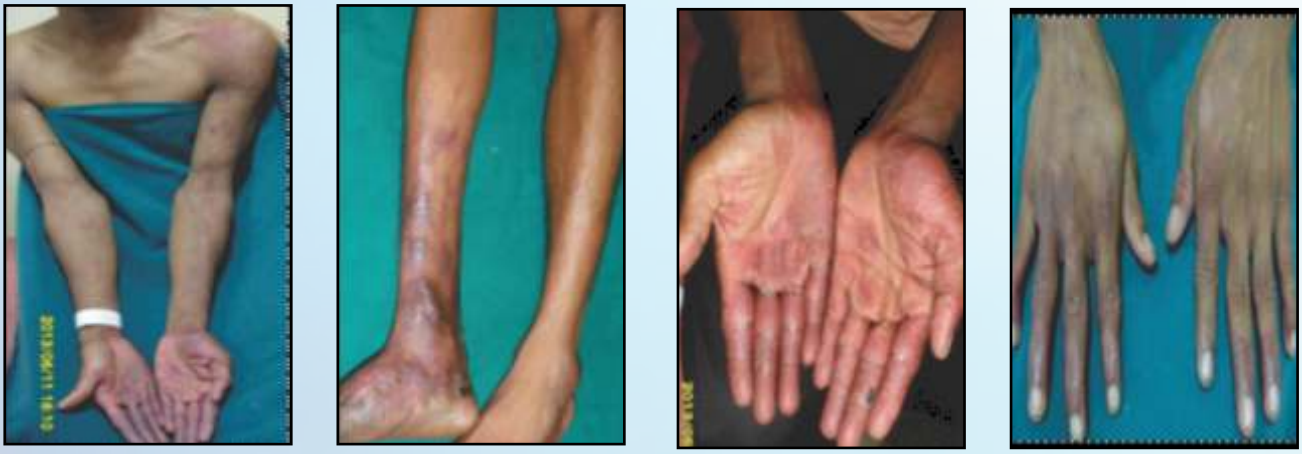
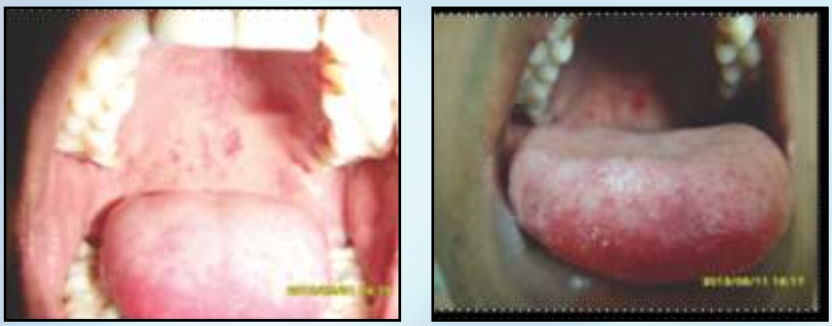
CASE REPORT

Port wine stain seen bilaterally over upper and lower limbs A 20 year old male presented with multiple extensive capillary malformation involving the entire upper & lower limbs, since birth. Multiple punctate telangiectasia were noted over tongue and hard palate. Secondary verrucous changes were seen over right leg and foot ocular examination revealed conjunctival telangiectasia. Fundus fluorescein angiography revealed multiple retinal telangiectasia with AV malformations and minimal leak. Colour doppler of AV malformations showed slow-flow type. CT contrast brain, USG abdomen, endoscopy and colonoscopy reports were normal



Port wine stain seen bilaterally over upper and lower limbs

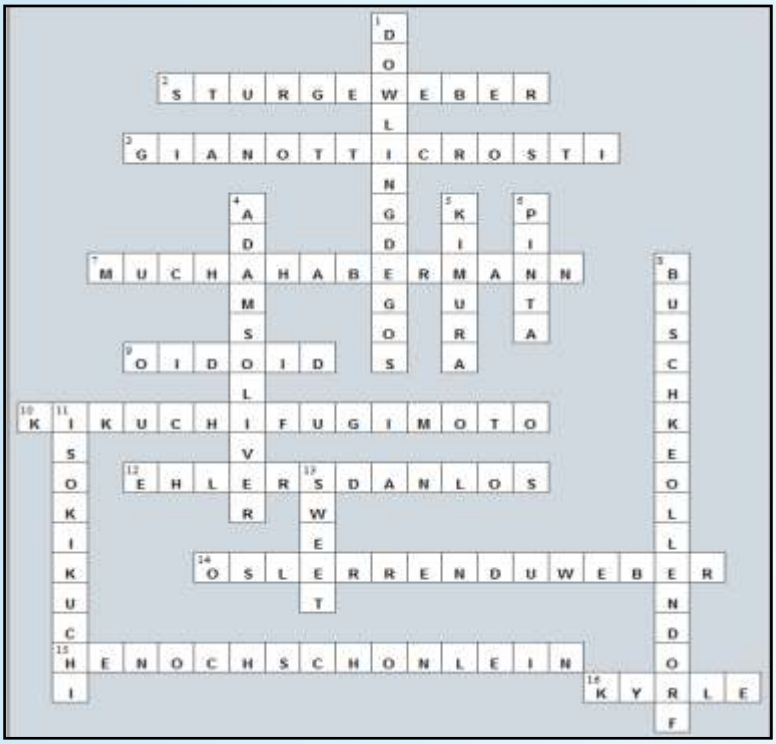


Multiple punctate telangiectasia present over tongue and hard palate

What is your diagnosis?

(Answers to Quitz on Page No.20)

8. ANSWERS TO CROSS WORD



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7. ANSWERS TO CASE REPORT & QUIZ

Capillary malformation- Arteriovenous malformation (CM-AVM)

DISCUSSION

Multiple vascular malformations frequently occur in association with systemic involvement. In this case, however there were multiple lesions which exhibited only secondary cutaneous changes and retinal involvement in the form of multiple retinal telangiectasia and arteriovenous malformations with minimal leak and exudates. CM-AVM has to be chiefly differentiated from hereditary hemorrhagic telangiectasia (HHT) and hereditary benign telangiectasia (HBT). The points against HHT and HBT were the absence of family history, presence of lesions at birth with very few telangiectasias and the absence of systemic involvement

REFERENCE

1. Eerola, I., Boon, L. M., Mulliken, J. B., Burrows, P. E., Dompmartin, A., Watanabe, S., Vanwijck, R., Vikkula, M. Capillary malformation-arteriovenous malformation, a new clinical and genetic disorder caused by RASA1 mutations. Am. J. Hum. Genet. 73: 1240-1249, 2003

NEWS & EVENTS

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