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AN OVERVIEW ON LEPROSY

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1. INTRODUCTION

Leprosy is also known as hansen's disease it is chronic and highly contagious infectious disease caused by Mycobacterium (M.leprae) or mycobacterium lepromatosis (M.lepromatosis) ,that affected the skin, muscles, nerve , mucous membrane , peripheral nerves , and other part of body, but it mainly affected on the nerves which result in serious disabilities. leprosy disease are seen in patient since the bible time. over the 3000 years ago. there are no clue that where leprosy originated . term leprosy are originated by the Norwegian physician Gerhard Armauer hansen and it also identified bacillus mycobacterium leprae.(1) in most of cases, it transfer from one individual to another through contact with patients that have a high bacillary record and that haven't been Treated.(2)

According to WHO in 2005 leprosy are eliminated through world health problem . Due to the introduction of multiple drug therapy (WHO/MND) in 1982 , using the clofazamine ,Dapsone and rifampicin has shorted the effective treatment of leprosy but due the increased in population in the western world leprosy may starting spreading and due to the immigrant's live under poor & crowd condition leprosy spread more rapidly.

The mode of spread of M. Laprae or M.lepromatosis the mode of spread of leprosy is not definitely determined but it possible to spread via :-

(1) Breast milk

(2) Air bone spread

(3) Biting insects.

The main symptom of leprosy is skin lesion , discoloured patches of skin , thick stiff or dry skin , loss of eyebrows or eyelashes.

2. DIAGNOSIS

It is disease of peripheral nerve and the mucosa particularly the upper respiratory tract. the leprosy is diagnose under the clinical signs and symptoms.

Skin lesion is the first main symptom of leprosy and because of skin lesion it is considered that it is dermatological disease. untreated leprosy may cause permanent damage to skin, nerve , limbs , and the eye also the tissue damage may occur (3). Due to immunological reaction most of the damage is secondary and also sensory loss may occur (4). The WHO considers one cardinal sign enough in endemic nations advantageously failing to remember the nerve enlargement. The more than 100 years known cardinal indications of uncleanliness are:

1. Loss of sensation in a skin sore
2. Enlarged fringe nerve
3. Positive skin spread

Though the diagnosis of leprosy is mostly clinical , there are a number of laboratory and clinical tests that can help support the clinical diagnosis by providing bacteriologic , histopathology, and immunologic information.(1) (2) (3) (4)

1. Histopathology:

Histopathology is the diagnosis and study of tissue . Generally all patient are diagnosed to have leprosy have lesions examined histopathologically . Histopathology is hallmark of tuberculoid leprosy.

2. Slit skin smear:

This was once the cornerstone of successful MDT implementation ;(5)(6)(7) however , its stubborn unreliability , interoperate variability , and lack of reproducibility in different hands , as well as the high risk of AIDS transmission when performed under difficult is field conditions, have eroded its importance even in WHO guidelines .Scrapes the sides of slits cut in the skin around the lesions (s),earlobes ,eyebrows and fingers .These scrapings are then ziehlnNeelsen's technique and high magnification for acid fast bacilli.

3. Lepromin test (skin test):

The Lepromin skin test is used to determine the type of leprosy a person has contracted. it is also known leprosy skin test. it is also use for determine the patients immunologic condition . it is measure of a person hypersensitivity to M. lepare antigen , which might be integral lepromin , Dharmendra antigen , leprolin.

4. Immunocytochemical techniques:

Negative neuropeptide staining gives indirect evidence of dermal nerve injury.(8)(9) By indicating nerve injury or loss (S100, methenamine silver) and remnants/traces of M. leprae (immunofluorescence / immunoperoxidase), these techniques this technique used in the diagnosis of leprosy in cases when histology is inconclusive.

5. Serology:

Serologic assays can detect antibodies to M. leprae(10)(11) specific antigens or antigens themselves, such as phenolic glycolipid-1 (PGL-1); however, the approach is time-consuming and cannot be used routinely for every leprosy patient and/or contact, and it is not widely available. PGL-1 antibody titers seem to represent a patient's bacillary burden, and they can be used to follow up on patients to see how well chemotherapy (11) is working; however, such assays have not been proven to be an efficient tool in the early identification of leprosy in high-risk persons. (12)

6. Immunofluorescence:

The fluorescent leprosy antibody absorption test is one of the sensitive tests for determining subclinical infection in patients and contacts, as well as predicting the likely course of the disease when used in conjunction with lepromin(13). However, the procedure is technically demanding, which, combined with its low specificity, has kept it from becoming widely used.

7. Cytopathology:

Because of its simplicity, minimal resource demand, quick results, reproducibility, and reliability that approaches that of histology, cytopathology is gaining acceptance as a diagnostic tool in leprosy in a few sites (where accessible). In a bacillary / paucibacillary form of leprosy, cellular evaluation serves as an across-check, boosting diagnostic reliability; nonetheless, it requires a technical team trained in the use of skin cytopuncture and/or needle aspiration for leprosy assessment, as well as the right mindset.

8. Polymerase chain reaction:

The polymerase chain reaction, which detects M. leprae specific DNA segments, is perhaps the most sensitive and specific method for confirming the presence of M. leprae DNA in any tissue/fluid sample; however, it is only available in specialised laboratories and requires a significant amount of money and expertise to perform. As a result, it is not widely available and is frequently impractical for everyday usage in the field for challenging cases.(14)

9. Chemotherapy:

Specific treatment, including the WHO-recommended MDT, has been the key tool in the fight to break the cycle of leprosy transmission and reduce the disease's prevalence in society.(15)(16) This has proven to be the most effective part of the eradication campaign, and whatever progress obtained has been attributed to the regime's effectiveness as well as the design's robustness. There is still a need for an effective, shorter-duration regimen for improved compliance and easier supervision, as well as for alternate medications for resistant infections and to eliminate persisters.(17-21)

TREATMENT:

Table 1: Important achievements in the Leprosy therapy

Late nineteenth century- until the 1940s	Use of chaulmoogra oil in the treatment of Leprosy [22,23]
1940	Promin, a sulfone drug, was introduced as a treatment for leprosy [24,25]
1941	Dapsone was first used by Faget, et al. for the treatment of leprosy in Carville, Louisiana, USA [26,27]
1955	National Leprosy Control Programme (NLCP) was launched in India to control the number of leprosy

	infection [28]
1964	The emergence of resistance to dapsone [29]
1970	Identification of Rifampicin as a new and effective anti-leprosy drug [30]
1981	WHO recommended the use of MDT [31]
1983	National Leprosy Eradication Program (NLEP)was launched in India [32]
1983	Introduction of MDT in India
1992	RO* for 28 days (daily) [33]
1994	WHO-MDT (FDT*-24) [34]
1995	ROM-12 for MB, ROM-6 for PB
1996	WHO-MDT (FDT-12 for MB and FDT-6 for PB)
1997	ROM-1 for 1 day (single dose) [35]
2000	WHO calls for the elimination of leprosy [36]
2005	Elimination of Leprosy in India as a public health problem at the national level in December 2005 [37,38]

figure.1

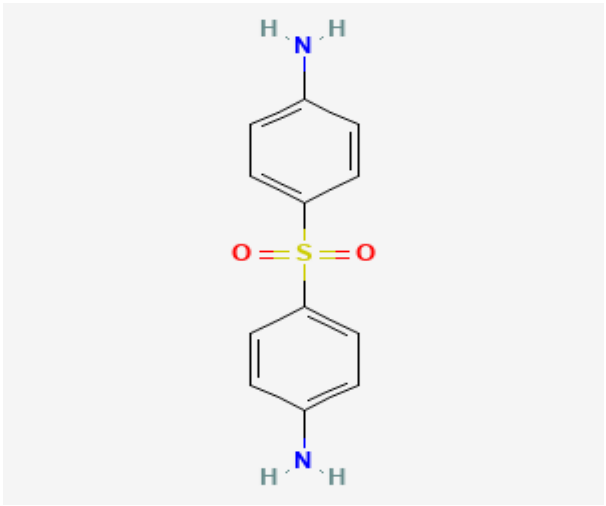
from the above table (1) chaulmoogra oil , recorded in sushruta samhita 600 BC, was the first known treatment used for the leprosy. chaulmoogra might have calming effect and fever reducing properties. in 1943 first effective intravenous promin or sodium glucosulfone apperead. after that new oral derivate dapsone (diaminodiphenyl sulfone , DDS) use in the treatment.

First line antibiotics:-

1. Dapsone (diaminodiphenyl sulfone)

In 20th centuries dapson are invented by the German chemist paulehrich while working on selective toxicity. Dapsone (diamino diphenyl sulffone) is medication most commonly used in combination with rifampicin & clofazimine as multi drug therapy (MDT) for treatment of mycobacterium lepare (leprosy). it official in IP, BP,USP.

structure:-



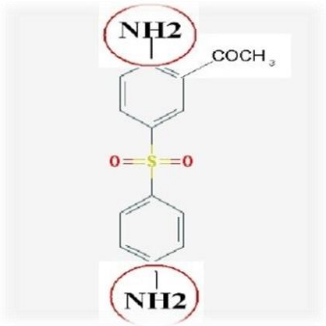
4,4'- diaminodiphenylsulfone

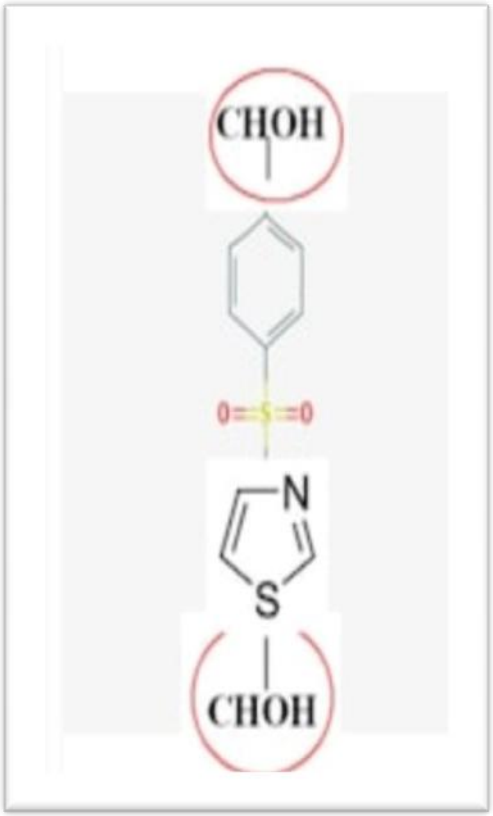
SAR :-

Substitution of aromatic ring with acetyl group result in decreased activity increased solubility in water and decreased G.I irritation.

Replacement of 1 amino group with nitro, hydroxy or hydroxylamine result in decreased activity Replacement of both amino group ithaldehyde result in prodrug formation (eg. glucosulfone sodium).

Replacement of one of benzene ring with thiazole results in decreased activity.





Dapsone is bacteriostatic, meaning it inhibits the growth of bacteria and protozoa. In 1940, dapsone antimycobacterial activity was established for the first time in the treatment of tuberculosis. Dr. Guy Faget of the National Hansen Disease Center in Carville, Louisiana, demonstrated the amazing effects of Prominin in the treatment of leprosy in the 1940s, ushering in the current era of leprosy therapy(39). It has been discovered that with significant treatment, leprosy progression is not accompanied by traditional pathologic cellular alterations. Promin (glucosulfone sodium) was the first sulfone to be employed in the treatment of leprosy instead of the parent substance dapsone, which was thought to be too toxic and very promising result but it administered intravenously. Cochrane successful treated leprosy patients with 1.25 g subcutaneous dapsone twice a week in 1947.(40) Oral dapsone, 100 mg daily, was the standard leprosy treatment in 1951, and it was widely used as monotherapy in the 1950s and 1960s. The dose of 100 mg

dapsone is weakly bactericidal against M.Leprae, but active lesions improve after a few weeks of treatment. Dapsone (sodium sulfoxone),Promacetin (aceto-sulfone), and a range of other sulfones that may be supplied orally safely were developed as a result of further research.

RIFAMPICIN:

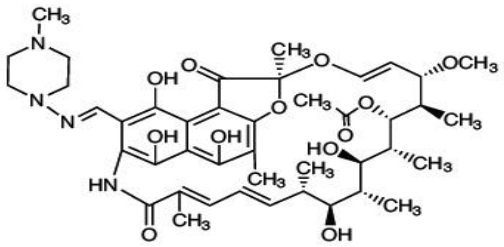
Rifampicin, like all other leprosy medications, is a member of the rifamycin group and was first employed as a tuberculosis treatment. Rifampicin is the only anti-leprosy medicine with a high bactericidal effect that renders the MDT mine w patient non-infectious within days of starting treatment.(41) The medication is also effective against microbes that produce dapsone. In mycobacteria, rifampin inhibits RNA synthesis by binding to the B-subunit of the RNA polymerase encoded by RpoB.(42) In 1970, the first investigations were undertaken to support the efficacy of rifampicin against susceptible M. leprae strains, as well as resistant strains to dapsone.(43)

Patients in the first clinical trial were given a daily dose of 600 mg of rifampicin, but the WHO recommended switching to a monthly dose in 1982 because "the increased effectiveness of the 600 mg daily dose of rifampicin compared to the 600 mg monthly dose" had not been demonstrated, and there was a need to monitor the use of Campicin because it was more cost effective at the time [6]. Unfortunately, the thrilling usefulness and advantage were quickly eclipsed by the emergence of resistance, which was induced by a mutation in the Rpo B gene [7]. The absence of rifampicin resistance in more than 10 million patients who completed MDT could be attributed to two factors.

1. Post - MDT monitoring for relapse has been discontinued.

2. Rifampicin susceptibility testing is difficult to carry out.

Structure:-



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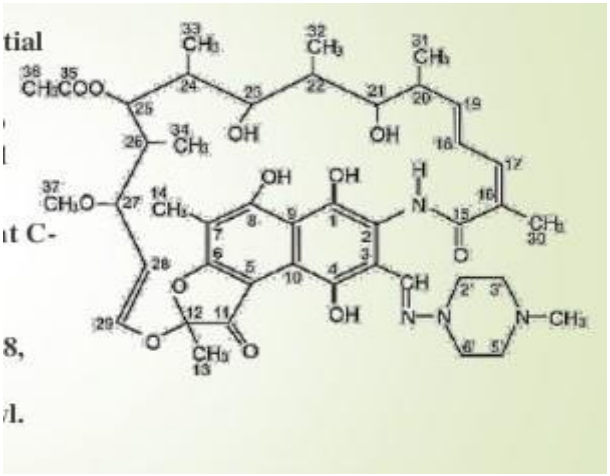

1) Intact macro cyclic molecule is essential for activity.

2) Saturation of double bond in macro cyclic ring leads to slightly decreased activity.

3) Free hydroxyl (-OH) group present at c-1, c-8,c-21,c-23 are essential for activity.

4) Substitution of hydroxyl group at c-8,c-21,c-23 lead to loss of Activity ; except c-1 from hydroxyl to carbonyl.

CLOFAZIMINE:

Clofazimine was first used as a leprosy monotherapy in the early 1960s and remained in use until the mid-1970s. Clofazimine, like dapsone, is bacteriostatic and slowly bactericidal against M. leprae, but the mechanism of its action is unknown. The medicine may work by inhibiting DNA;s template function, enhancing lysosomal enzyme synthesis, and improving macrophage phagocytic capability.Resistance to clofazimine is uncommon,despite its sluggish onset, which could be owing to its various modes of action. Clofazimine;s main drawbacks include increased skin pigmentation and dryness (ichthyosis), both of which occur as the medicine becomes more clinically effective.

MDT (multiple drug therapy):

The WHO Studies Group recommended the MDT, dapsone, rifampicin, and clofazimine in 1981. In compact blister packages for the monthly calendar, this combination is safe and effective. Since 1995, the World Health Organization has provided free MDT to all patients globally. The therapy for MB leprosy is recommended to last 12 months. This treatment group includes patients with lepromatous leprosy (LL), borderline leprosy (BL), and borderline-borderline (BB) leprosy, as described by the Ridley and Jopling method.

Clinical presentations	**Population**	**Agents**	**Dosing regimen**	**Treatment duration**
Paucibacillary leprosy	Adults	Rifampicin Dapsone	600 mg/month 100 mg/day	6 months
	Children	Rifampicin Dapsone	450 mg/month 50 mg/day	6 months
Multibacillary leprosy	Adults	Rifampicin Clofazimine Dapsone	600 mg/month 300 mg/month and 50 mg/day 100 mg/day	12 months

	Children	Rifampicin Clofazimine Dapsone	450 mg/month 150 mg/month and 50 mg/day 50 mg/day	12 months

Table 2: Standard multidrug therapy regimens for paucibacillary and multibacillary leprosy in adults and children (WHO)

On the basis of field trials and clinical research, the WHO Expert Committee on Leprosy has concluded that a single dosage of rifampicin, ofloxacin, and minocycline is an acceptable and cost-effective alternative for the treatment of single lesion paucibacillary leprosy. They also indicate that the MDT regimen for multibacillary leprosy could be shortened to 12 months.

Multidrug therapy (MDT), which was first recommended by a WHO Expert Committee in 1984 and has been provided free of charge to all endemic countries by WHO since 1995, has quickly become the standard treatment for leprosy.(8)

REFERENCES

[1] Eidt LM. Breve história da hanseníase: sua expansão do mundo para as Américas, o Brasil e o Rio Grande do Sul e sua trajetória na saúde pública brasileira. Saúde Soc. 2004;13:76-88

[2] Talhari S, Penna GO, Gonçalves HS, Oliveira MLW. Aspectos Gerais da Hanseníase, Agente Etiológico, Transmissão, Patogenia, Classificação, Manifestação Clínica, Diagnóstico. In: Talhari S, Penna GO, Gonçalves HS, Oliveira MLW. Hanseníase. 5. ed. Di Livros: Rio de Janeiro; 2015. p.1-94-17

[3] Sehgal VN, Rege VL, Reys M. Correlation between clinical, bacteriological and histopathological classification of leprosy. Int J Lepr 1977;45:278–80

[4] Sehgal VN. Clinical criteria for diagnosis of Hansen's disease. The Star 1990;49:14–6

[5] . Anonymous (Report of a WHO Study Group). Chemotherapy of leprosy for control programmes (Tech Report Series No. 675), Geneva: World Health Organization, 1982.

[6] Sehgal VN, Joginder. Slit-skin smear in leprosy. Int J Dermatol 1990;29:9–16.

[7] . Sehgal VN, Koranne RV, Sehgal S, et al. Correlation of morphological bacteriological and histopathological features of leprosy: Double-blind study. J Dermatol 1985;12: 243–50.

[8] Fleury RN, Bacchi CE. S-100 protein and immunoperox idase technique as an aid in the histopathologic diagno sis of leprosy. Int J Lepr 1987:55:338-44

[9] Sekar B, Sharma RN, Anandan D, et al. Indeterminate leprosy: A seroimmunological and histochemical evalu ation. Lepr Rev 1994;65:167-77.

[10] Klatser PR. Serology of leprosy. Trop Geog Med 1994;46: 115–8.

[11] Prakash K, Sehgal VN, Aggarwal R. Evaluation of phenolic glycolipid-1 (PGL-1) antibody as a multidrug therapy (MDT) monitor. J Dermatol 1993;20:16–20

[12] Chanteau S, Glaziou P, Plichart C, et al. Low predictive value of PGL-1 serology for the early diagnosis of leprosy in family contacts: Results of a 10-yr prospective field study in French Polynesia. Int J Lepr 1993; 61:533–41

[13] Bharadwaj VP, Katoch K. Detection of subclinical infection in leprosy: An 8 years follow-up study. Int J Lepr 1989;61:495–502

[14] Santos AR, Nery JC, Duppre NC, et al. Use of the polymerase chain reaction in the diagnosis of leprosy. J Med Microbiol 1997;46:170–2

[15] Anonymous (Report of a WHO Study Group). Chemo therapy of leprosy for control programmes (Tech Repor Series No. 675), Geneva: World Health Organization, 1982.

[16] Anonymous (Report of a WHO Study Group). Chemo therapy of leprosy (WHO Tech. Rep. Ser. No. 847), Ge neva: World Health Organization, 1994;1-24

[17] Pattyn SR. Search for effective short course regimens for the treatment of leprosy. Int J Lepr 1993;61:76–81

[18] Waters MFR. Relapse following various types of multidrug the treatment of leprosy. Int J Lepr 1993;61:76-81. therapy in multibacillary leprosy. Lepr Rev 1995;65:1-9

[19] Grosset J. Whither short-course chemotherapy for lep rosy? Ind J Lepr 1997;69:119-20. 102. Sehgal VN, Jain S, Bhattacharya SN, Persisters, relapse (reactivation), drug resistance and multidrug therapy (MDT): Uniform diagnostic guidelines for leprosy are needed. J Dermatol 1996;23:905-7.

[20] Desikan KV. The risk of relapse after multidrug therapy in leprosy. Lepr Rev 1997;68:114-6.

[21] Anonymous. Risk of relapse in leprosy. (WHO Doc. WHO/CTD/LEP/94), Geneva; World Health Organiza tion, 1994.

[22] Cottle W (1879) Chaulmoogra oil in leprosy. Br Med J 1: 968-969.

[23] Dos Santos FSD, De Souza LPA, Siani AC (2008) Chaul moogra oil as scientific knowledge: The construction of a treatment for leprosy. Hist Ciencias Saude Manguinhos 15: 29-47

[24] Faget GH, Pogge RC, Johansen FA, Dinan JF. Prejean BM (1966) The Promin Treatment of Leprosy. A Progress Re port. Int J Lepr Other Mycobact Dis 34: 298-310.

[25] Trautman JR (1984) A brief history of Hansen's disease. Bull N Y Acad Med 60: 689-695

[26] Nicholls L (1922) Treatment of leprosy. Br Med J 2: 892

[27] Faget GH, Pogge RC (1946) Present status of promin treat ment in leprosy. Int J Lepr 14: 30-36.

[28] Desikan KV (2012) Elimination of leprosy & possibility of eradication the Indian scenario. Indian J Med Res 135: 3-5.

[29] Pettit JHS, Rees RJW (1964) Sulphone resistance in lep rosy. An experimental and clinical study. Lancet 284: 673 674.

[30] Rees RJW, Pearson JMH, Waters MFR (1970) Experimental and clinical studies on rifampicin in the treatment of lep rosy. Br Shams Med J 1: 89-92.

[31] WHO (1982) Chemotherapy of leprosy for control programmes.

[32] Shetty S. Shetty JN (1997) National Leprosy Eradication Program Indian J Dermatol 42 55-64

[33] World Health Organization (2012) WHO Expert Committee on Leprosy World Health Organ Tech Rep Ser 1-61,

[34] Ishi N. Barua S. Mari S, Nagaoka Y. Suzuki K (2010) Report of the tenth meeting of the WHO technical advisory group on leprosy control Nihon Hansenbyo Gakkai Zashi 79:37-42

[35] Shinde A Khopkar U, Pai VV (2000) Single-dose treatment for single lesion leprosy: Histopathological observations. Int J Lepr Other Mycobact Dis 68: 328-330

[36] WHO (1996) Global strategy for the elimination of leprosy as a public health problem.

[37] Elimination of leprosy Resolution of the 44th World Health Assembly Geneva World Health Organization 1991 Reso lution No (2018) Appl Sc 8: 2-5.

[38] World TF. Assembly H. WHA51.15 Elimination of leprosy as a public health problem (2000) 15-16

[39] Faget GH, Pogge RC, Johansen FA, Dinan JF, Prejean BM (1966) The Promin Treatment of Leprosy. A Progress Report. Int J Lepr Other Mycobact Dis 34: 298-310.

[40] 40.Coachrane R, Ramanujam K, Paul H, Russell D (1949) Two-and-a-Half Years Experimental Work on the Sulphone Group of Drugs. CABI 20: 4-64.sy.

[41] Shepard CC, Levy L, Fasal P (1972) Rapid bactericidal of fect of rifampin on Mycobacterium leprae. Am J Trop Med Hyg 21: 446-449.

[42] References Scollard DM, Adams LB, Gillis TP. Krahenbuhi JL. Truman RW. et al. (2006) The continuing challenges of leprosy, Clin Microbiol Rev 19: 338-381

[43] Rees RJW, Pearson JMH, Waters MFR (1970) Experimen tal and clinical studies on rifampicin in the treatment of lep rosy. Br Shams Med J 1: 89-92.