REGIONAL MEETING ON LEPROSY
MOGADISHU 25 - 28 February 1980

EM/MTG. LEP/4
24 February 1980

REGIMENS RECOMMENDED ACCORDING TO THE CLINICAL CLASSIFICATION AND BACTERIOLOGIC CONDITIONS OF CASES

by Dr J. Languillon

1. I have been requested to talk about treatment recommended in the field for leprosy in relation to classification. In this connection I may be permitted to remind that it is the immunological status of patients, that is to say, the presence or otherwise of cell mediated immunity to M. leprae, which results in the clinical form of the disease. This is reflected in the appearance of specific cutaneous lesions and in the preseance or absence of M. leprae in the nasal mucosae or in the derma.

The following is what happens when a subject is exposed to virulent bacille:-

- If the exposed person had already had either a leprosy or a tubercular infection, and has developed a good cell mediated immunity response, the M.leprae are rapidly destroyed after penetration in the organism.

- If the cell mediated immunity response is weak, the disease will start and present itself in what is known as an indeterminate form. This form is transitory and of relatevely short duration. It occurs essentially in children and adolescents. This form will evolve according to the immunity response of the individual into:-

a) Tuberculoid form if the patient has a stable cell mediated in response though weak at moment of contact) likely to reinforce itself in the case of the infections. The mycobacteria leprae enter into the dermal nerves inducing the formation of leprides and in the large nerve trunks producing nevritis and thereafter paralysis specially of the face, hands and feet, bone lesion and plant or ulcers.

b) Lepromatous forms if the patient presents a total and permanent cell mediated immunity deficiency, the bacilli of the M. leprae multiplies inside the histiocytes invading the whole organism and in particular the skin, specially the mucosa of the nose, larynge and farynge, the nerves, the eye the lymphoglands, some visceral organs and some endocrine glands.

c) Interpolar forms (French classification including borderline forms which may shift to either tuberculoid or lepromatous).

This form has an unstable equilibrium and a patient may clinically deteriorate "down-grade" into a lepromatous form through an intermediate status of a borderline tuberculoid form. Conversely the patient may recuperate partially his immunity response and upgrade into a tuberculoid form from a borderline lepromatous(reversal reaction)

2. In the field visual diagnostic methods are sufficient for the classification of the patients. This based on 7 cutaneous criteria and one bacteriological criterion as follows:-

1. Definition of the margins of the lesion
2. Alteration of sensibility at the level of the lesion
3. Affections of skin appendices such as hair, eyebrow, and sudoriporous glands
4. Aspect of surface of the lesion
5. Distribution of the lesions
6. Presence or absence of central atrophy
7. Lesions of peripheral nerves
8. Presence or absence of M. leprae at microscopic examination of mucosa and skin.

The field medical auxiliaries can reach a dignostic through visual observation and microscope, almost on the totality of the cases. Such diagnostic of the clinical form will lead to the most appropriate treatment.

2.1 Intermediate forms

1. Margin rather not well defined
2. Loss of sensitivity to heat and pain
3. Hypohydrosis (loss of perspiration at the area of the lesion)
4. Flat surface of the hypochromic macula
5. 1 to 5 maculae with asymmetric distribution
6. Absence of central atrophy
7. No lesion in the peripheral nerves
8. Generally absence of M. leprae in the mucosa and skin specimens

2.2 Tuberculoid form

1. Clear delimitation of the dermal lesion
2. Considerable loss of sensitivity (anaeastesia, to heat and pain)
3. Unhydrosis and loss of hair at the level of the lesion
4. Micro papular iniltration of the surface
5. 1 to 5 asym m etric leprides
6. Frequent centrat atrophy
7. Asymmetric hypertrophic palpable nerves
8. Negtive for M. leprae at microscope examination of mucosa and skin specimens.

2.3 Lepromatous form

1. Lack of clear limits of lesion
2. Normal sensitivity
3. Loss of hair and eyebrows
4. Surface infiltrated shiny with greasy appearance
5. Symmetric distribution of lepromes
6. No central atrophy
7. Painful hypertrophy of nerves with symmetrical distribution
8. Large numbers of M. leprae in globy (nasal mucosa and dermal fluids).

2.4 Interpolar forms

1. Unclear limits of the lesion with a halo around the lesion
2. Often lack of sensitivity to heat and pain
3. Anhidrosis , no hair loss
4. Micropapular in filtration with colour tending to red, violet, shining
5. Many lesions with tendency to symmetry
6. No central atrophy but immune zones (central areas of normal skin)
7. Symmetric hypertrophy of nerves with paralysis with rapid onset and evolution
8. M. leprae present (particularly in forms evolving towards lepromatous (down grading)

3. Available drugs showing effective results

3.1 The sulphone group

The 4 4' diaminodyphenyl sulphone (DDS) also known under the name of dapsone was sentetized in 1908 but utilized by Faget in 1941.. It is usually available in form of tablets of 100 mgs (disulone). It is also available in an injectable formulation as a suspension in 5 ml. of ethyl ester oil of chaulmoogra of 1.250 gr (DDS). The standard dosage is established in relation to the weight of the patient as 1.5 mg/kilo/day or 10 mg/kilo/ week, or intramuscular injection 20 mg/kilo/twice a month.

It was recommended that treatment should start with a progressively increasing dosage, but the present practice is to start straight with the full dosage.
The sulphone group has low toxicity, is absorbed by the small intestin and is eliminated through the urines. The reported collateral effects include exfoliative dermatitis hepatitis, aneemia. The most frequent complication is erythema nodosum leprosum. (ENL). This occurs in about 40% of treated cases.

The action of dapsone in the initial stage of treatments is bateriostatic. After a few months it seems to acquire bacteriocidal properties. It may be assumed that the large antigenic charge could, in the presence of circulating antibodies, cause the ENL as an Arthus phenomena. The efficacy of dapsone is proved in the bacilli ferous form by a fall of the morphologic index (MI) to zero in 6 months, and by clinical and bacteriological recovery in 3 to 5 years. In the tuberculoid form its action is slow with aggravation of the nevritis.

3.1.1 The sulphone preparation which has a delayed absorbtion is the 4 4' diacetyl-diamonophenyl commenly known as DADDS or HAN SOLAR. It is administered with intramuscular injections of 225 mg every 70 days. The constant presence in the organism of a certain load of the drug may lead to the induction of the resistence. Furthermore should ENL reaction occur it would be necessary to wait until the complete elimination of the drug in order to obtain remission of the cause of the reaction.

Consequently full symptomatic treatment would be required for a long time. The constant presence of the drug is proven by the regular elimination of about 2 to 3 mg per day.

It is very difficult to envisage therefore the utilization of this drug as a mass treatment but it may be advisable as maintainance treatment after recovery as well as prophylaxis of lepromatous cases.

3.2. The retard sulphamide drugs used in leprosy are the sulphamethoxypyridazine (sultirene, lederkin) and sulphadimethoxine (madribon). These are administered at a dose 750 mg every 2nd day but experience has shown that in mass treatment sulphortomidine or fanasil would be preferable at a weekly dosage of 1.5 gr.

The above drugs would be probably give some good results in bacilliferous forms but at present their use is confined to tuberculoid and interpolar forms with neverities. Uptil now there is no evidence of cutaneous reations.

3.3 Clofazimine (Lamprene, B 663)

This is phenazine presented in form of a yellow powder in capsules of 100 mg, it has a clear specific action resulting in the fall of the morfologic indenx to zero in 6 months and disappearance of M. leprae from the lesions as well as an improvement in the cutaneous lesions as observed in DDS treatment. The dosage consists of 100 mg/day or 600 mg /week or 1 gr. at one time in a month for an adult of average weight. The advantage of lamprene over dapsone is that there are no ENL reactions reported up to date. It is also effective on M. leprae ressistant to sulphone and sulphamides. In fair skinned patients a reddish colorarion of the lesion may be observed.

3.4 Riphampicin

This is an antobiotic derived from streptomices mediterraenei, it is a very powerful bactericide for M. leprae. It is presented in 300 mg capsules as a brickred powder.

The action of riphampicin consists in the block of ARN polymerase which is essential. for the synthesis of M.leprae.

The drug is absorbed by the intestinal tract, concentrated by the liver where it is progressively degraded and by loss of the acetyl group does acquire a very strong bactericidal power. The elimination of the drug is partly through the bile and the stools for about 30% while 20% are eliminated through the kidneys.

Following experimentation of various dosages, the following regemins have been suggested:-

a) 1200 mg /1 month/ 6 months

b) Single dose of 1500 mg not repeated. This latter single dose treatment has brought the morphological in dex to zero in the first month which means that all forms of M. leprae revealed in the mucous and dermal fluids are granular and non viable. In practice the patients are rended non infectious within one month of the first single dose treatment. The advantages of the single dose is that it is well tolerated. This is important considering the intermittent treatment or continous treatment used by some workers (eg. 400 mg/day/ 4 weeks) can provoke cutaneous and gasto intestinal reaction, hepatic lesion thrombocitopenic purpura, haemolytic anaemia, fall of blood pressure, shock or simply grippelike reactions.

4. Summary of various regimens of treatment according to clinical form.

4.1 Indeteminate: DDS 100 mg/day (1,5 mg/kilo/day) adult dose

4.2 Tuberculoid : As above.

4.3 Tuberculoid with nevritis: Sultiréne 750 mg every second day or fanasil 1,5 gr once a week

4.4 Borderline tuberculoid and borderline lepromatous:

Lamprene 100 mg/day (adults dose) associated with sulphamide (sultirene) 750 mg on alternative days and Ducton one intramuscular injections every second day (Ducton is a lisate of neissaria perflava and or stimulaut of cell mediated immunity)

4.5 Lepromatous:

Rifampicin 1200 mg/ 1 month / 6 months and clofazimine 100 x 1 mg x 6 months plus DDS 100/ day for the whole life.

The above is a combined treatment recommended for cases resistence to Dapsone. It should continue throughout the life so that " persistent bacilli" in the liver, the nerves , nerve sheath, bones, and some muscles might be prevented to re-establish the previous bacillary charge.

4.6 ENL in lepromatous case treated with DDS

While some workers prefer to coutime DDS, I prefer to replace this with clofazimine at 100 mg or more per day according to the extent of reaction. Thalidomide can also be administrated in man at a dose of 6 mg/kg/day during one week. In women corticosteroid should be given rather than thalidomide. Dosage must be decided depending on effectiveness.

When reaction has been controlled, it is advisable to continue clofazimne for 6 months at a stand of 100 mg/ day at the end of the 6 months a return to sulphone treatment at lower dosages of 50 mg/ day can be resumed.

4.6 Lepromatous cases with M. leprae to DDS

Multiple treatment is recommended in this case as follows:-

- 6 rehampicin 1200 mg/ 1 month/ 6 months
- clophazyme 100 mg/ 1 day through all life
- ethionamid

This subject will be discussed by another speaker who will provide you with more details in this status of treatment of resistent cases.