DOUBLE BLIND PLACEBO CONTROLLED STUDY TO EVALUATE THE EFFICACY OF ANTIBIOTIC / DEC OR BOTH TO PREVENT ADL IN *Wuchereria bancrofti* FILARIASIS

WHO / TDR FUNDED PROJECT

START : **MARCH 1995**
END : **DECEMBER 1998**

VECTOR CONTROL RESEARCH CENTRE

(INDIAN COUNCIL OF MEDICAL RESEARCH)

PONDICHERRY

OBJECTIVES

- To evaluate the efficacy of administration of proposed doses of oral antibiotics or DEC or both in the prevention of episodic ADL attacks in patients with bancroftian filariasis in a double placebo controlled study

- To relate clinical consequences of the above treatment with immuno-pathological changes.

- To study the involvement of aerobic bacteria in the causation of ADL and their antibiotic sensitivity

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DESIGN: 5 Armed double blind design

Treatment components	ARMS				
	1	2	3	4	5
Oral Penicillin *	+	-	+	-	-
Oral DEC**	-	+	+	-	-
Oral Placebo	-	-	-	+	+
Local antibiotics	+	+	+	+	-
Local placebo	-	-	-	-	+
Foot care ***	+	+	+	+	+
Local Anti fungal cream	+	+	+	+	+

* 800,000 I.U. per day

** 50 mg single dose daily

*** Washing the affected limb daily in the morning and before to bed using soap and water

DISTRIBUTION OF RECRUITED CASES BY DRUG CODE, GRADE AND GROUP

DRUG CODE	GROUP I			GROUP II		
	GRADE 1	GRADE II	TOTAL	GRADE III	GRADE IV	TOTAL
A	3	12	15	13	2	15
B	2	12	14	14	2	16
C	2	13	15	14	1	15
D	3	13	16	14	0	14
E	3	13	16	14	0	14
TOTAL	*13*	*63*	*76*	*69*	*5*	*74*

DRUG COMPLIANCE ACCORDING TO DRUG CODE, GROUP AND GRADE

DRUG GROUP	% DRUG CONSUMED		
	GROUP I	GROUP II	ALL
A	74.8	89.1	87.6
B	69.3	88.6	85.6
C	80.4	87.1	83.6
D	80.1	88.3	83.7
E	81.9	79.3	80.8

$$\% \text{ Consumption} = \frac{\text{Mean number of days drug consumed}}{\text{Mean number of days drug should have been consumed}} \times 100$$

IMPACT OF THERAPY ON MEAN ADL FREQUENCY

Intervention group	Group I Cases			Group II Cases		
	Pre	During	Post	Pre	During	Post
DEC	3.38	0.56	0.38	4.57	1.21	0.21
Penicillin	4.07	0.36	0.50	4.38	0.38	0.25
Penicillin + DEC	3.20	0.13	0.20	4.93	0.33	0.33
Placebo + local Antibiotic	4.20	0.87	0.27	3.13	1.47	0.53
Placebo	3.94	0.25	0.31	3.43	1.00	0.29

IMMUNOHISTOPATHOLOGY COMPONENT

Rationale: Strategy for morbidity management

Objective: To understand the pathogenesis to develop appropriate therapy

Design: Skin biopsy from 150 lymphoedema patients

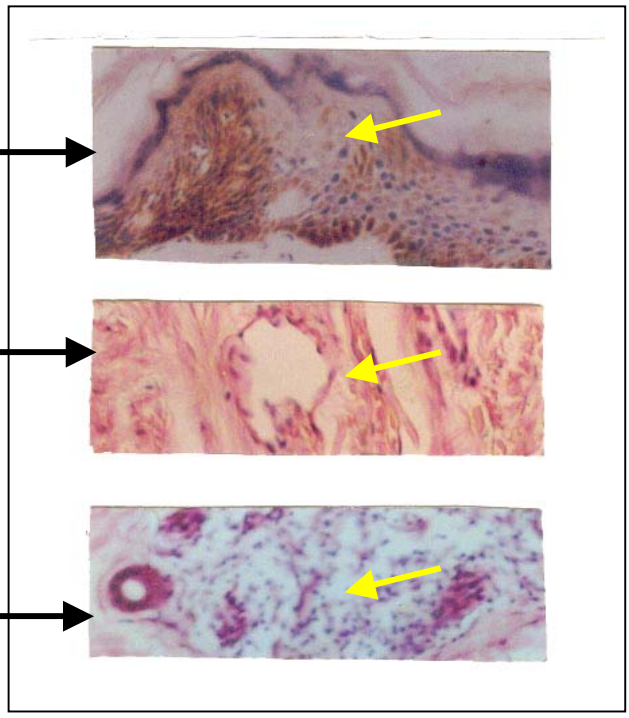
Staining: a) Haematoxylin and Eosin b) Peroxidase Anti-peroxidase (PAP) using monoclonals for langerhan's cells, Pan T-cells macrophage, HLA-DR and Vimentin

Histopathology of filarial lymphoedema

Epidermis:
Hyperkeratosis (H&E: 100x)

Dermis: Dilatation of lymphatic capillaries (H&E, 100x)

High mononuclear infiltration particularly around blood vessels (H&E, 100x) but not around lymphatics,



Hyperproliferation and dilatation of blood capillaries, increased number of fibroblast

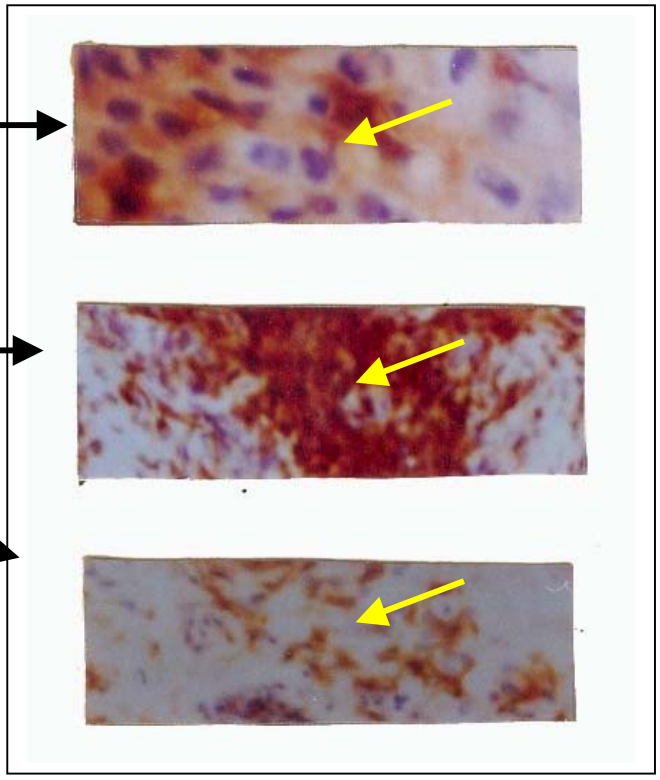
IMMUNOHISTOPATHOLOGY OF FILARIAL LYMPHOEDEMA

Epidermis: Increased number of Langerhan's cells (CD1; PAP; 400x)

Dermis: Increased number of Pan T-cell, (CD3; PAP 100x)

Macrophage (CD 68; PAP 100x)

Immunocompetent cells and Vimentin in dermis



Conclusion:

- Observed increased thickness of epidermis and hyperproliferation of dermis
- Infiltration of mononuclear cells is evident around blood caopillaries but not around dilated lymphatic capillaries.
- Findings indicate pathogenesis due to external antigenic stimuli

Application: Foot care hygiene could reduce the progression of filarial lymphoedema. This knowledge is useful for morbidity management

CONCLUSIONS

1. **Foot-care alone results in reduction of acute adenolymphangitis attacks in bancroftian filarial lymphoedema cases**

2. **Isolation of Group A Beta haemolytic *Streptococci* was significantly higher in ADL cases.**

3. **Histo-pathological and immuno-histo-pathological changes suggest chronic inflammation, particularly from external sources.**