Chemotherapy reduces human anti-filarial IgE response

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The effect of diethylcarbamazine treatment on levels of IgE antibodies to infective larval (L_3) antigen of *Wuchereria bancrofti* and to a purified allergenic fraction (Sd_{30}) of *Setaria digitata* was followed up to 1 year in asymptomatic microfilaraemic patients infected with *W. bancrofti*. IgE levels increased transiently by day 15, followed by marked decline beginning at one month and persisting up to 12 month post-treatment. IgE responses to Sd_{30} underwent greater changes compared to L_3 antigen of *W. bancrofti*.

FILARIAL infection leads to an enhanced production of IgE antibodies in humans. The serum levels of specific IgE in different categories of *Wuchereria bancrofti* infection have been determined[1,2]. The highest level is exhibited by patients with chronic infection, followed by clinically normal people residing in the endemic regions and asymptomatic microfilaraemic carriers (AS). Immunologic changes in microfilaraemic (MF) patients associated with treatment with diethylcarbamazine (DEC), the drug of choice in filariasis, have been studied[3,4]. Chemotherapy brought about enhanced cellular immune responsiveness[5]. Changes in the antibody isotypes, especially IgE, have not received adequate attention. We report here the effect of DEC treatment in MF patients on levels of IgE antibodies to a purified allergenic fraction of *Setaria digitata* adult worms and to somatic infective larval (L_3) antigen of *W. bancrofti*. The allergenic fraction, which has been shown to cross-react serologically with L_3 antigen, exhibits IgE profile in filarial patients similar to that of L_3 antigen[6].

The study population was from a *W. bancrofti* endemic region of Orissa (Khurda district), India[2]. Eighteen microfilaraemic individuals of both sexes, aged 19–46 years (median 25 years), wishing to participate in chemotherapy were given DEC orally for 12 days at 6 mg/kg body weight under the supervision of a local medical officer. Blood samples were collected 15 days, 1, 3 and 8 months and 1 year after treatment. All the individuals were MF-negative when checked at 1 month post-treatment. L_3 antigens of *W. bancrofti* and the allergenic fraction of *S. digitata* (designated as Sd_{30}, molecular weight 30 kDa as determined by SDS-PAGE and G-200 Sephadex Gel filtration) were prepared as described earlier[2,6]. Serum IgE levels (at 1/100-fold dilution) were determined by ELISA by coating the plates with high antigen concentrations. The procedure was followed as described earlier[2].

All patients had measurable levels of IgE antibodies to both antigens before treatment. Changes in levels of IgE antibodies after DEC treatment relative to pretreatment levels are shown in Figure 1 and Table 1. A significant increase ($P < 0.05$) was noticed by day 15 in IgE response to Sd_{30} antigen. This was followed by a sharp decline, leading to values considerably lower than pretreatment values. The reduction observed at 1 month reached a nadir around 3 months after treatment and then increased progressively. The enhancement on day 15 was noticed in all patients except in four (two unaltered; two decreased). At 3 months, 15 patients exhibited a reduction in IgE response to Sd_{30} antigen, ranging from 72 to 100%; only two patients showed 50% and 20% drop. One patient did not exhibit any change after therapy. Levels of IgG antibodies to these antigens were, however, not affected (data not shown) by DEC treatment. All patients were found to remain amicrofilaraemic at 1 year post-treatment. It is of interest to note that IgE levels registered an enhancement at 1 year from the lowest values obtained at 3 months post-treatment.

Levels of IgE antibodies to Sd_{30} allergen underwent

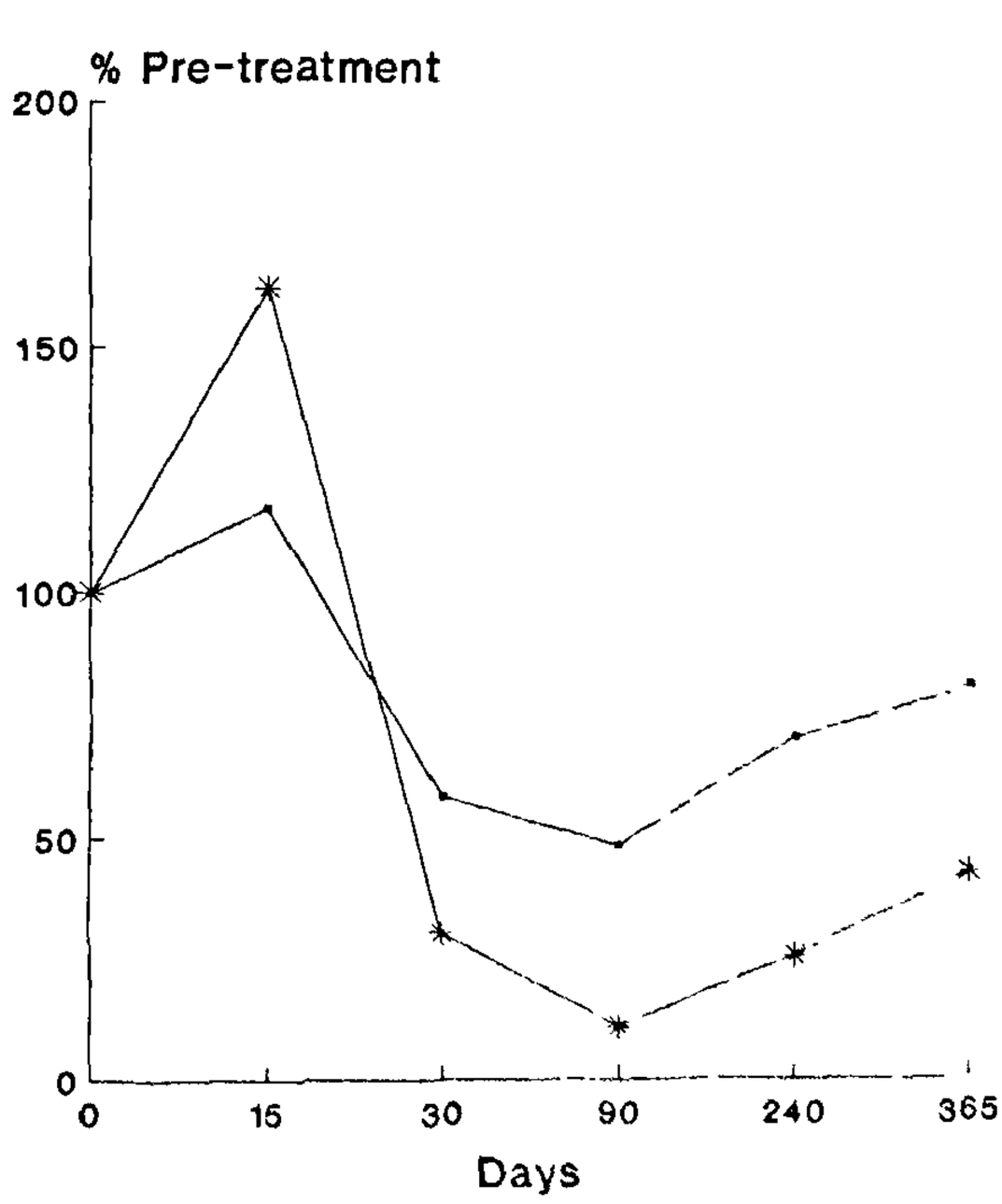

Figure 1 Antifilarial IgE levels after DEC treatment expressed as percentages of pretreatment for each patient. Each point represents the mean value of change with respect to pretreatment response for individual patients. (*) Sd_{30}, (o) L_3 antigen

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Table 1. IgE levels (ELISA $A_{492} \pm SD$) in microfilaraemic patients ($n = 18$) after diethylcarbamazine treatment

	A_{492}					
	Pretreatment	Days posttreatment				
Antigen	Day 0	15	30	90	240	365
Sd_{30}	0.22 ± 0 10	0 36 ± 0 16 **	0 06 ±0 04 *	0 02 ± 0 02 *	0 05 ± 0 04 *	0 08 ± 0 06 *
W. bancrofti L_3	0.34 ± 0 10	0 40 ± 0 22 NS	0 19 ± 0 11 *	0.16 ±0.10 *	0.24 ± 0 13 *	0 30 ± 0 18 NS

**$P < 0 05$ compared to day 0; *$P < 0 01$ compared to corresponding day 0 or day 15.
NS. not significant compared to day 0

greater changes than those to *W. bancrofti* L_3 antigen. For example, the mean reductions in IgE response to Sd_{30} and L_3 antigen 3 months after treatment were 90% and 50% of pretreatment values, respectively. The lower reduction in L_3-IgE may be caused by persistent exposure to *W. bancrofti* larvae in the endemic region. It might also be possible that DEC treatment induces changes in IgE response to epitope(s) selectively present in Sd_{30} allergen. Earlier we have demonstrated that IgE response to these antigens is filariae-specific since people living in nonfilarial regions of Orissa exhibited negligible IgE levels[2 6]. IgE production is sustained in people in endemic areas by them being continuously exposed to the infection since clinically normal individuals of the endemic region have high IgE levels[2].

Considering the biologic roles of IgE antibodies in parasite infections, which vary from allergic disorders to conferring protection to hosts[7,8], the effect of drug treatment on IgE response is an interesting topic. The changes in specific IgE levels as reported here have not been characterized in human filariasis. The present report describes the response of the levels of IgE antibodies to two different antigens, L_3 stage of *W. bancrofti*, which initiates the infection, and a purified filarial allergen, Sd_{30}. Both the antigens exhibited diminished IgE production in treated patients over a course of time.

Immunologic changes following a two-year community trial of ivermectin treatment in Guatemala of patients infected with *Onchocerca volvulus* have been reported[9]. Enhanced parasite-specific IgE levels were noticed 6 months after treatment, which fell marginally below the pretreatment level by the second year. Although antiallergic action of DEC is well documented[10–12], the underlying mechanism was not known. The present results demonstrate clearly that DEC treatment diminishes the production of filarial IgE antibodies in humans and thereby contributes to decreasing allergic reactions.

The long-term monitoring of the study population will be helpful in finding out when IgE levels would be generated again in the DEC-treated patients.

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Biochemical basis for the differentiation of the two nonpoisonous snakes *Eryx conicus* Schneider and *Eryx johnii* Russell (family: Boidae)

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The tissue-specific patterns of lactate dehydrogenase (LDH) for two species of the genus *Eryx* are reported and characterized utilizing sodium deoxycholate. LDH-1 is predominant in *Eryx conicus*, whereas LDH-3 and LDH-2 are observed in *Eryx johnii*. Sodium deoxycholate is a selective inhibitor of LDH-5 in *Eryx johnii*. Variations are observed in all the tissues between these two species and there is a variability of tissue LDH expressions within the species.

ISOENZYMES are multiple molecular forms of enzymes[1]. They can serve in taxonomic, genetic, phylogenetic and