IMMUNITY TO DIPHTHERIA IN WOMEN OF CHILDBEARING AGE IN DELHI IN 1994: EVIDENCE OF CONTINUED *CORYNEBACTERIUM DIPHTHERIAE* CIRCULATION

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Abstract. Blood samples from 171 full-term pregnant women (aged 18-38 years) of middle socioeconomic status from Delhi were tested for diphtheria antitoxins by indirect hemagglutination (IHA) test. History of primary immunization/clinical diphtheria during childhood was not ascertainable, but none had been revaccinated against diphtheria at any time. About 94% women had very high antitoxin titers (≥ 0.125 IU/ml); none had antitoxin titer less than 0.015 IU/ml, the minimum protective level. The titers were uniformly high in all age groups. However, women having 2 or more children had significantly higher antitoxin titers than those having no or one child ($p < 0.01$). The results from this study and historical data on diphtheria in Delhi are compatible with continued transmission of *C. diphtheriae* in recent times in Delhi which is of sufficient magnitude to boost the antitoxin levels in adults, especially mothers having two or more children. The study highlights the need of increasing the immunization coverage with DPT among children to reduce the transmission of *Corynebacterium diphtheriae*.

INTRODUCTION

Recent outbreaks of diphtheria in the newly Independent States of the former USSR (EPI, 1995a) which mainly affected the adult population, have raised concern about the susceptibility of adult populations in other countries also. Before contemplating measures to prevent the spread of outbreak in other areas, it is necessary to check immunity levels in adult populations to determine whether a large number of susceptible adults indeed exist in the community (EPI, 1995b). The present study was undertaken for this purpose.

MATERIALS AND METHODS

Two private maternity centers situated in congested localities of east and west Delhi participated in the study. The subjects were full term pregnant women who were admitted for delivery in these centers during October 1993 to January 1995. They were 18-38 years old and most of them were literate housewives. They belonged to middle socioeconomic status and their families had the capacity to pay for their deliveries. However, they lived in areas inhabited by people of all socio-economic strata. They were interviewed with respect to age, parity and immunization after childhood. History of primary immunization or clinical diphtheria was not ascertained because its authenticity was likely to remain doubtful in most cases.

Blood samples were drawn by venipuncture and transported to the laboratories of the National Institute of Communicable Diseases (NICD), Delhi on ice. The sera were separated and stored at -20°C till tested for diphtheria antitoxins by indirect hemagglutination test (Ray *et al,* 1978a). A level of 0.015 IU/ml was considered as a minimum protective level (Weiss *et al,* 1983). As has been suggested (EPI, 1995b), the mothers were grouped in 3 classes on the basis of antitoxin titer:

(1) < 0.015 IU/ml = unprotected

(2) 0.015-0.06 IU/ml = uncertain protection status

(3) ≥ 0.125 IU/ml = definitely protected

Under laboratory based surveillance, throat swabs from clinically suspected diphtheria cases from the Infectious Diseases Hospital (IDH), Delhi were processed in the laboratories of NICD for isolation of *Corynebacterium diphtheriae* (Anony-

mous, 1984). The data for the period 1973-1994 also formed the material for this study. In addition, historical data on clinical diphtheria in IDH during 1954-94 (Anonymous, 1976; Patnaik and Kapoor, 1967; Shastri, 1985) and estimates of coverage levels with 3 doses of DPT in different immunization coverage surveys undertaken in Delhi (Chadha and Trivedi, 1986; DGHS, 1980, 1982; EPI, 1993; Gupta and Murali, 1989; Varshney, 1988) were also used to interpret the results.

The results were analysed by software Epi Info version 5.

Table 1

Diphtheria antitoxin titers in pregnant mothers in Delhi.

Titer (IU/ml)	No. of subjects	Percentage
< 0.015	0	0
0.015	1	0.6
0.030	3	1.8
0.060	7	4.1
0.125	28	16.4
0.25	49	28.7
0.50	50	29.2
≥ 1.0	33	19.3
All titer	171	100.0

RESULTS

As shown in Table 1, all the 171 women had antitoxin titers ≥ 0.015 IU/ml. Of the total, 160 (94%) had high antitoxin levels *ie*, ≥ 0.125 IU/ml. Table 2 shows the antitoxin titers at different ages. An increasingly higher proportion of the older subjects had antitoxin titers ≥ 1.0 IU/ml. However, the differences among the age groups were not statistically significant ($p > 0.5$). The data on the antitoxin levels at different parity are shown in Table 3. Of the 38 mothers who had 2 or more children, 37% had antitoxin titers ≥ 1.0 IU/ml, whereas only 15% and 13% of those having none or one child, respectively, had such high antitoxin titers. The differences were highly significant ($p < 0.01$).

DISCUSSION

Diphtheria vaccine-induced immunity wanes over time (EPI, 1995b). It has been predicted that 25 years after primary vaccination, 25% of vaccinees would be unprotected (Kjeldsen *et al*, 1985). In addition, the reduction in the reservoir of *C. diphtheriae* subsequent to large scale immunization of children results in the reduction in opportunities to build up or maintain immunity against diphtheria through natural exposure to *C. diphtheriae* (EPI, 1995b). Therefore, in the absence of a circulating *C. diphtheriae* in nature or a revaccination program against diphtheria, many adults will have low or unprotective antitoxin levels

Table 2

Diphtheria antitoxin in pregnant mothers at different ages.

Age of mothers	Titer (IU/ml)				Total
	< 0.015	0.015-0.06	0.125-0.5	≥ 1.0	
18-24	0	6 (7)	67 (77.9)	13 (15.1)	86 (100)
25-29	0	4 (6.8)	43 (72.9)	12 (20.3)	59 (100)
30-38	0	1 (4.8)	15 (71.4)	5 (23.8)	21 (100)
All ages	0	11 (6.6)	125 (75.3)	30 (18.1)	166 (100)

Note: Age of 5 women was not ascertained.
Figures in parentheses are percentages.

Table 3

Diphtheria antitoxin in pregnant mothers in relation to parity status.

Parity	Titers (IU/ml)				Total
	< 0.015	0.015-0.06	0.125-0.5	≥ 1.0	
0 (first pregnancy)	0	4 (6.1)	52 (78.8)	10 (15.2)	66 (100)
1	0	7 (10.9)	49 (76.6)	8 (12.5)	64 (100)
≥ 2	0	0	24 (63.2)	14 (36.8)	38 (100)
All	0	11 (6.5)	125 (74.4)	32 (19)	168 (100)

Note: Parity of 3 women was not ascertained.
Figures in parentheses are percentages.

against diphtheria (Ad-hoc Working Group, 1978; Kjeldsen *et al*, 1985, 1988; Weiss *et al*, 1983). In fact, low immunity against diphtheria has become a general problem among adults in the western world (Kjeldsen *et al*, 1988). In contrast, adult populations in Delhi have been repeatedly shown to have diphtheria antitoxin titers ≥ 0.01 IU/ml which is considered to be the minimum protective level (Ichhpujani *et al*, 1993; Kumar *et al*, 1981; Ray *et al*, 1978b) (Table 5). In the present study also, all the subjects had uniformly high antitoxin titers in all age groups (Tables 1, 2). In the absence of a revaccination program in India, their immunity seems to have been boosted by natural infection - apparent or inapparent.

The data on the antitoxin titers at different parity (Table 3) provide a probable mode of transmission of *C. diphtheriae* in adult women. A significantly higher proportion of mothers having 2 or more children had antitoxin titers ≥ 1.0 IU/ml than those having none or one child. By the time a woman becomes full term pregnant for the third time, the older child is sufficiently mobile to catch diphtheria infection outside his/her home. Since women in general and mothers in particular remain in close contact with these young children, their immunity is also likely to be boosted by transmission of a subclinical infection.

The historical data on clinically suspected diphtheria in the IDH (Fig 1), isolation rate of *C. diphtheriae* from these cases in the laboratories of NICD (Fig 2), DPT3 coverage estimates in immunization coverage surveys (Table 4), and age distribution of cases are also compatible with a continued circulation of *C. diphtheriae* in recent times in Delhi which seems to be of sufficient magnitude to boost the antitoxin titers in the adult population.

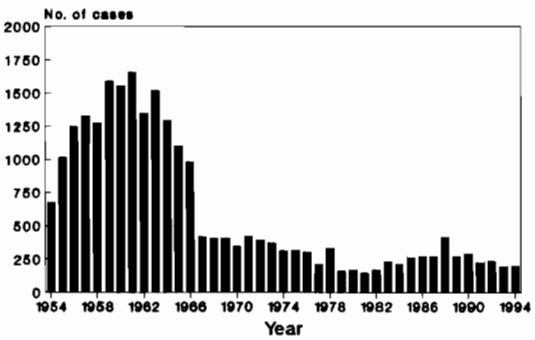

Fig 1–Clinically suspected diphtheria in Infectious Diseases Hospital, Delhi 1954-94.

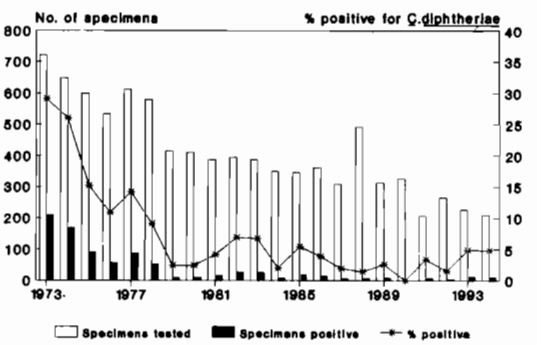

Fig 2–Culture positivity for *C. diphtheriae* in Delhi, 1973-94.

Table 4

DPT 3 coverage estimates in immunization coverage surveys (12-23 months) in Delhi.

Year	Place	Coverage DPT 3 (%)	Reference
1978	10 MCW center areas	55	DGHS, 1980
1979	Shakurpur	34	DGHS, 1980
1980*	Resettlement Colonies	22	DGHS, 1982
1980	Model Town	82	DGHS, 1982
1980	South Delhi	72	DGHS, 1982
1982	Trans Yamuna	52	DGHS, 1982
1986	Shahdara, Tilak Nagar, Tagore Garden, Subzi Mandi	72	Chadha and Trivedi, 1986
1988*	Whole Delhi 12 zonewise surveys	57-92 (Median 84)	Varshney, 1988
1989*	Delhi (urban)	74	Gupta and
*	(rural)	72	Murali, 1989
1990	Civil Line Zone	91	Unpublished
1991*	Delhi (All JJ Colonies)	54	EPI, 1993
*	(All Resettlement Colonies)	76	EPI, 1993
1991	Shakurpur (ICDS Block)	67	Unpublished
1991	Inderpuri (ICDS Block)	85	Unpublished

* Surveys in very large geographical areas

Table 5

Diphtheria antitoxin sero-surveys in Delhi by IHA test.

Year	Subjects examined	Age group	% having titer ≥ 0.01 IU/ml	History of previous vaccination	Reference
1976	662	Adults	96	No	Ray *et al*, 1978b
1980	1552	Adults	97	No	Kumar *et al*, 1981
1990-92	574	Adults (males)	88	NA	Ichhpujani *et al*, 1993
1993-94	171	Adults (females)	100	NA	Present study

NA = History of immunization not ascertained.

(i) Although diphtheria is showing a diminishing trend, ~200 clinically suspected cases continued to be admitted in IDH every year in 1990s (Fig1).

(ii) *C. diphtheriae* has been isolated from throat swabs of some clinically suspected cases every year (Fig 2). The low isolation rate may be due to early prescription of antibiotics before hospitalization and collection of clinical samples. Further studies are under progress to study the low isolation rates of the organism.

(iii) Most of the positive or suspected cases continue to occur in young children. For example, 46% of 196 suspected cases in 1994 were recorded

in 1-4 year age group (Panda *et al*, 1995), whereas 9 of 10 isolates of *C. diphtheriae* were recovered in the same period from under fifteen children (NICD, unpublished data).

(iv) As shown in Table 4, a coverage of as low as 54% and 76% with 3 doses of DPT was estimated in Juggi Jhopri and Resettlement (slum) colonies of Delhi respectively, in 1991. These slums provide shelter to a majority of the population, especially the poor, in Delhi. Keeping in view a less than 100% vaccine effectiveness and some problems in maintaining the cold chain, a substantial proportion of children remain susceptible to diphtheria and may allow a continuous transmission of *C. diphtheriae* infection.

The results suggest that there is at present no need for artificial boosting of immunity in the adult population in Delhi. Even if there is some gap of immunity in some adult populations, this may not be sufficient to sustain an outbreak unless coupled with low immunization rates in the child population (EPI, 1995b). Therefore, the obvious need is to achieve and maintain high immunization coverage with DPT among children to reduce the *C. diphtheriae* circulation. After sufficient reduction in *C. diphtheriae* circulation, properly timed booster doses of vaccine among adolescents and adults may need to be introduced in the EPI to avoid possibility of diphtheria outbreaks in the adult population in future.

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