

## Resurgence of Diphtheria: Are We ready to treat?

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### ABSTRACT

**Objectives:** To create awareness amongst the medical faculty about a forgotten fatal disease (diphtheria). To determine the age distribution, immunization status, presenting features, prognosis with respect to duration after which they took medication and effect of ADS on recovery in cases of faucial and laryngeal diphtheria. To stress on the importance of DTP immunization to control diphtheria.

**Study method:** In this study, 15 patients who presented to the Government general hospital between July and September 2013 with membranous tonsillitis were enrolled. In every diphtheria-proven case, we administered antidiphtheric serum (ADS) as early as possible along with injection crystalline penicillin (CP) and oral erythromycin. Tracheostomy was done in two cases who presented with stridor. Patient variables and their correlation with recovery were studied.

**Results:** Out of 15 cases of membranous tonsillitis, nine tested positive for diphtheria; eight, smear positive and one, culture positive. Of these nine cases, eight were between 9 and 13 years old and one was a 50-year-old man. While tracing immunization status, it was found that three children (33%) were not immunized, four children (22%) had not taken booster doses, and in one child and the adult, immunization history was unknown. Clinical presentation of two of the unimmunized cases was late (on 8th day of fever), with stridor due to laryngeal diphtheria. The third child presented with bull neck, and developed myocarditis. These three cases proved fatal. Six cases which presented early and were managed in time recovered fully.

**Conclusion:** Unimmunized children as well as adults are susceptible to diphtheria. High immunization coverage is the only tool to control this infection. Booster doses are needed to control disease in adults. It was found that early diagnosis with high index of suspicion and early administration of ADS along with good supportive therapy carried good prognosis. Every otolaryngologist, pediatrician as well as general practitioner should be ready to manage the cases of diphtheria. Government should be prepared to manage and control epidemics effectively.

**Keywords:** Faucial diphtheria, Laryngeal diphtheria, Immunization (DPT), Antidiphtheric serum.

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### INTRODUCTION

Diphtheria is a dreadful disease caused by *Corynebacterium diphtheria*, which is a Gram-positive, unencapsulated, nonmotile, nonsporulating bacillus.<sup>1</sup> It has a characteristic club-shaped bacillary appearance and three forms cluster of parallel rays (palisades) that are referred to as Chinese

characters. Human isolate of *C. diphtheriae* may display non-toxicogenic or toxicogenic phenotypes. Growth of toxicogenic strains under iron limiting conditions lead to optimum expression of diphtheria toxin and these conditions are believed to be a mechanism of pathogenesis during human infection. Bacilli are transmitted through respiratory droplets. Diphtheria is more commonly seen in children (>6 months to <15 years) and in unimmunized adults. Incubation period is 2 to 5 days. Bacilli usually multiply in the throat, elaborating exotoxin, which is responsible for local as well as systemic effects. The former includes pseudomembrane over tonsillopharyngeal region and less commonly lesions in the larynx, nares and trachea or bronchial passages. Large pseudomembranes are associated with severe disease and a poor prognosis. Mortality rate is 5 to 10%. A few patients develop massive swelling of the tonsils and present with as bull neck, which results from massive edema of the submandibular and paratracheal region and is further characterized by foul breath, thick speech and stridorous breathing. The diphtheritic pseudomembrane is gray or whitish and sharply demarcated. Unlike the exudative lesion associated with streptococcal pharyngitis, the pseudomembrane in diphtheria<sup>2</sup> is tightly adherent to the underlying tissues. Attempts to dislodge the membrane may cause bleeding. Hoarseness suggests laryngeal diphtheria, in which case, laryngoscopy may be diagnostically helpful. Systemic manifestations of diphtheria stem from the effects of diphtheria toxin and include weakness as a result of neurotoxicity and cardiac arrhythmias or congestive heart failure due to myocarditis. Clinical diagnosis is made by the constellation of sore throat, adherent tonsillar, pharyngeal or nasal pseudomembranous lesions and low grade fever. In addition, diagnosis requires isolation of *C. diphtheriae* or histopathological isolation of compatible Gram-positive organisms.

### HISTORICAL PROFILE OF DIPHTHERIA

Diphtheria is a very old disease. Its first clinical description was made by Hippocrates in the 4th century BC<sup>3</sup> and there are references of it in ancient Syria and Egypt. In the pre-vaccination era, the disease was distributed throughout the world, causing epidemics and pandemics regularly, with high mortality. Huge epidemics of diphtheria swept across Europe in the 17th century. In Spain, it was given the nickname 'El Garatillo', which means the strangler, and both Italy and Sicily knew it as 'the gullet disease'. By the 18th century, the disease made it to the Americas and reached epidemic

levels by 1735. It was not uncommon for whole families to die from the disease in just a few weeks (1778-1862). French physician Pierre Breteanu called it ‘diphtherite’.<sup>3</sup> During the 1990s in the states of the former Soviet Union, a much larger diphtheria epidemic<sup>4</sup> caused >150,000 cases and >5,000 deaths. Clonally related toxigenic *C. diphtheriae* strains of the ET8 complex were associated with this outbreak. Given that the ET8 complex expressed a toxin against which the prevalent diphtheria toxoid vaccine was effective, the epidemic was attributed to failure of the public health infrastructure to effectively vaccinate the population. Beginning in 1998, the epidemic was controlled by mass vaccination programs. During the epidemic, the incidence rate was high among individuals from >15 years of age up to 50 years of age. Socioeconomic instability, migration, deteriorating public health programs, frequent vaccine shortages, delays in implementation of vaccination and of treatment in response to cases, and lack of public education and awareness were contributing factors in that outbreak.

**PRESENT STATUS IN WORLD**

**Developed Countries**

Near 100% immunization coverage has eradicated the disease from most of the developed countries.

**India**

In developing countries like India, it still continues to be a major public health disease due to poor immunization coverage. India has the highest number of unimmunized (DPT) children in the world—8.6 million, i.e. more than 1/3rd of unimmunized children in the world live in India only.<sup>6</sup>

Graph 1<sup>5</sup> shows the distribution of unimmunized (DPT3) children in world. More than 66% of these live in just 10 countries; 37.2% in India.

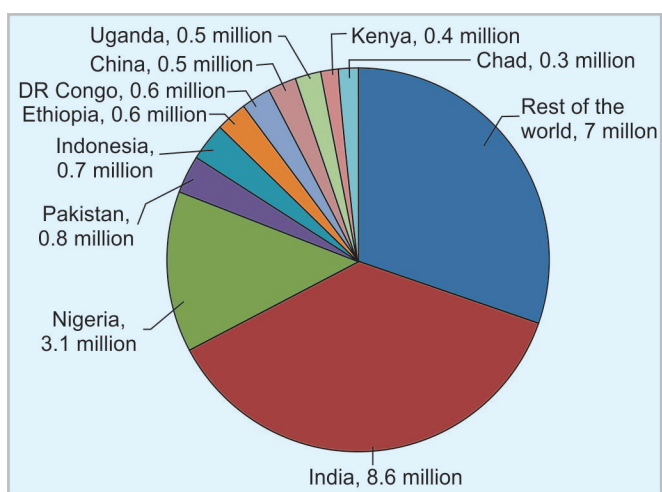
Not surprisingly, India has the highest number of diphtheria cases in the world.<sup>6,7</sup> These figures are 17 times higher than 2nd placed Indonesia (183). The following table shows number of reported cases in India in the past few years.

Year	2012	2011	2010	2008	2007	2006	2005	2004
Reported cases	2525	3485	3123	3529	3977	3812	2534	5826

All the above are reported cases. Majority go unnoticed, which means that the above may indicate only tip of iceberg! What about the true number of diphtheria cases?

**Andhra Pradesh**

The unbelievable fact is that in India, 71% of cases are from Andhra Pradesh (4,161 cases), as per 2004 statistics.<sup>8</sup>



**Graph 1:** Distribution of unimmunized (DPT 3) children in the world

In 2013, Synchronous with our surge (Kakinada) of cases, 44 cases of diphtheria had been reported in fever hospital, Hyderabad.

**Kakinada City**

No single case has been reported in the past 15 years but there is sudden surge of cases (9 cases) in the past 3 months (July 1, Aug 4 and Sep 4).

**MATERIALS AND METHODS**

The present prospective study was carried out on 15 patients who presented to the Department of ENT, eight Government General Hospital, Kakinada, East Godavari district head quarters, Andhra Pradesh, India, with membranous tonsillitis between July and September 2013. We took careful history about the onset and duration of symptoms, immunization status and meticulous clinical examination was done. In all cases, throat swabs were taken and sent for Albert’s staining and culture on Loeffler’s serum slope before antibiotic administration. Diphtheric antitoxin was administered (after checking for hypersensitivity) empirically to three cases. Out of these, two were laryngeal diphtheria cases which presented with stridor, fever and large membrane over tonsils, oropharynx and extending down into larynx; another, with bull neck and severe toxic features (Figs 1 to 3). In the remaining six cases, diphtheric antitoxin were administered after confirmation of smear for *Corynebacterium diphtheriae*. Injection crystalline penicillin (12,500-25,000 U/kg, IM, 12th hourly) as well as tablet erythromycin (40-50 mg/kg, 6th hourly) were given as antibiotics of choice in all cases.<sup>10</sup> Tracheostomy was done in two laryngeal diphtheric cases which presented with stridor. Hourly echocardiogram monitoring had been done in all cases. Whenever necessary, pediatrician opinion had been taken in the management. For all close contacts of cases, we advised tab erythromycin 250 QID for 10 days.



**Fig. 1:** Sunitha, 11-year-old female child, faucial diphtheria, grade 3 tonsils with pseudomembrane



**Fig. 2:** Viney Kumar, 12-year-old male child, faucial diphtheria, grade 3 tonsils with pseudomembrane



**Fig. 3:** Pooja, 12-year-old female child, laryngeal diphtheria, grade 4 tonsils with pseudomembrane

### Follow-up

We advised DPT vaccination at the time of discharge for all six cases which had complete recovery.<sup>9</sup>

### Notification

We informed about all cases immediately to district immunization officer and district health officers.

### Epidemiological Measures

After receiving the information regarding the cases of diphtheria, the health agency formed an outbreak control team, which collected complete data regarding the cases/deaths and confirmed the outbreak.<sup>11</sup> They took immediate

measures to identify the suspected cases and referred these to Government General Hospital, KKD. They also took measures to protect the at-risk population with DPT immunization by conducting a health camp at a high-risk area, Etimoga (a remote place in Kakinada).

### RESULTS

Out of 15 membranous tonsillitis cases, eight proved to be smear positive and one culture positive for diphtheria. Out of these nine cases, five were females and four males. The age of eight cases were between 9 and 13 years, and one was 50 years old. On tracing their immunization status, it was found that three children were not immunized, four children had not taken booster doses and, in one child and one adult, immunization history was unknown. Clinical presentation of two unimmunized cases were late (on 8th day of fever) with change in voice, difficulty in swallowing and stridor. On examination, both cases showed grayish membrane over the tonsils, posterior pharyngeal wall and extending down into larynx (laryngeal diphtheria). Despite early antidiphtheric toxin administration and timely tracheostomy, patients did not recover. Another unimmunized case presented late with bull neck had developed myocarditis on the 2nd day of admission (8th day of fever) and died. Six cases (1 adult of unknown immunization status and five children who had not received booster doses of DPT) who presented early with symptoms of sore throat and fever recovered fully with timely treatment.

### DISCUSSION

Diphtheria is an infectious disease caused by *Corynebacterium diphtheriae*. It was regarded as a dreaded disease throughout history and was also called 'strangling angel of child'. It is transmitted through respiratory secretions. Clinically, it may present as faucial (tonsil), laryngeal or cutaneous type. According to literature, laryngeal diphtheria has poor prognosis. In our study also, both laryngeal diphtheria cases died despite of adequate treatment (100% mortality). Similarly, all the cases (six) which presented early and received timely treatment recovered completely (100% recovery). So, every attempt should be made to diagnose the cases early. Creating awareness about this once forgotten disease in medical faculty and health officials will be essential not only to diagnose the cases early and manage them efficiently but also to prepare them for control of epidemics. Creating awareness amongst the people will help them to understand the benefits of vaccination and seeking treatment early. A multidisciplinary approach, involving a team of otolaryngologist, pediatrician and anesthesiologist is needed for optimum care of the patient. Every case should be notified to district health and immunization officers to know the burden of disease in the community. This will help



to implement epidemiological measures, which can lead to earlier diagnosis, identification of high-risk populace and control of further spread of epidemic. Diphtheria is a vaccine preventable disease; high immunization coverage (>90%) is the only tool to control the disease.<sup>12</sup>

### Future Research

It has been found that antitoxin 13 levels gradually fall<sup>13,14</sup> with age, and reach below protective level after 60 years. So, extensive studies are required to know about the number of doses and timing of administration of booster doses of dT vaccine in adults to maintain protective antitoxin levels (> 0.01) in the body.

### CONCLUSION

Diphtheria should be diagnosed with high index of suspicion on clinical basis. This will lead to early management which can ensure good prognosis. Although diphtheria is common in the 5 to 15 years age group, it can occur at any age. Especially during outbreaks, adults (19-65 years) are commonly affected. The most common presenting features of faucial diphtheria are fever and sore throat. Cases which present late and those with laryngeal involvement carry poor prognosis even with adequate treatment. Cases with bull-neck have more chance of development of myocarditis and also carry poor prognosis. The familiar proverb 'prevention is better than cure' applies here too. This means that the health agencies and the government will have to take maximum efforts to increase immunization coverage from present 50 to 60% to more than 90% and bring down the worst statistics of diphtheria.

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