

CLINICAL DIPHTHERIA IN THE NON-EUROPEAN

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Diphtheria is endemic in South Africa, a fact to which Bokkenheuser and Heymann¹ recently drew attention. In view of the high incidence of the disease, an assessment of its present clinical status in the non-European was considered worthwhile.

Material. This study is based on 1,135 cases of diphtheria (corrected for diagnosis) admitted to Waterval Hospital, the non-European Isolation Hospital of the Johannesburg Municipality, during the 3 years 1952-1954. The cases consisted of 1,017 Bantu, 75 Coloured, 41 Indians and 2 Chinese. Practically every case was personally seen by the author, and every bed-letter reconsidered in order to achieve uniformity at least in the diagnosis and classification of the cases presented.

Seasonal Incidence. During the months December to May 712 cases or 62.7% of the cases were admitted.

There were most admissions in January and February. This appears a constant feature in this country.

Sex Distribution. The cases comprised 631 females and 504 males. The slightly greater incidence of the disease amongst females appears to be universal.

Age Distribution is shown in Table I. The proportion of cases under the age of one year, viz. 6.4%, is more than 3 times as great as in the London Fever Hospitals in the years 1895-1914,² where it was 1.8%. The figures are probably comparable in that they are both taken from a non-immunized population, viz. that existing in

TABLE I. AGE DISTRIBUTION

<i>Age (years)</i>	<i>No.</i>	<i>%</i>		<i>Age (years)</i>	<i>No.</i>	<i>%</i>
Under 1	72	6.4	} 45.6%	7-11	223	19.6
1-3	199	17.5		11-16	98	8.6
3-5	246	21.7		16 and over	106	9.3
5-7	191	16.8		Total	1,135	99.9

London before the institution of active immunization, and our relatively non-immunized Bantu population. The proportion of cases in adults is nearly the same (10%) in the two series.

Almost half the cases (45.6%) occurred under the age of 5 years, the under-school age-groups. The London figure was 41.7%.

The youngest case was one of nasal diphtheria in a 12-day-old infant with a history of 7 days. The youngest case of faucial diphtheria was in an infant of 6 weeks; the oldest was in a female of 60 years.

History. To obtain an accurate history from an African adult is notoriously difficult; from an unaccompanied baby it is impossible. However, information was obtained in about 340 of the cases. The average duration of illness before admission to hospital was 4 days. Complaints in children were: feeling off-colour, refusal of feeds, some feverishness and often a sharp dry cough. Sore throat was only rarely mentioned, and the necessity of examining the throat regularly in a sick child cannot be over-emphasized. Adults invariably complained of a sore throat and slight constitutional disturbances. Pain, however, was usually not severe and had frequently disappeared even when membrane was still present.

The Type and Severity of Disease is shown in Table II. The types of diphtheria were classified as (1) nasal, (2) faucial, (3) laryngeal, (4) nasal and faucial, (5) faucial and laryngeal, (6) nasal, faucial and laryngeal, and (7) others (cutaneous, aural, conjunctival and vaginal).

TABLE II. TYPE AND SEVERITY

Type	No.	%	Grade	No.	%
Nasal	40	3.6	1st ..	343	30.2
Faucial	887	78.1	2nd ..	390	34.4
Laryngeal	20	1.8	3rd ..	402	35.4
Nasal and Faucial	95	8.3			
Faucial and Laryngeal	80	7.1			
Nasal, Faucial and Laryngeal	12	1.1			
Others	1	0.1			

Faucial diphtheria (alone) comprised nearly 80% of the cases, nasal diphtheria (alone) 3.5% (40 cases) and primary laryngeal diphtheria 1.8% (20 cases).

The 'other' types were extremely rare (a single case of cutaneous diphtheria); although ulcers secondarily infected from a virulent nasal discharge, and a case of purulent conjunctivitis secondarily infected in a similar way, did occur. There were no true cases of aural diphtheria, i.e., with membrane in the ear, but there were cases of chronic otitis harbouring virulent organisms in their aural discharges.

The severity of the disease was classified in 3 grades, corresponding to mild, moderate, severe, by a scheme which is a slight modification of Banks³:

Grade 1=membrane on one tonsil, or a small amount on both.

Grade 2=a larger amount on both tonsils, with (a) slight involvement only of uvula and pharynx or (b) an associated nasal or laryngeal involvement, and with cervical lymphadenitis present.

Grade 3=(a) membrane involving tonsils, uvula and pharynx, with an obvious peri-adenitis (bull neck), unilateral or bilateral, or (b) a severely toxic case, irrespective of the amount of membrane (the membrane may already have partially stripped by the time the case is admitted).

The 3 grades were more or less evenly represented, with slightly fewer mild cases. Grade 1 would comprise a higher proportion if all early cases were recognized and admitted to hospital.

Bacteriological proof was obtained in a disappointingly small percentage of cases (50%). Apart from faulty technique in taking the swabs and the delay in bacteriological examination (steps have since been taken to rectify these, with a significant improvement in results) the other factor responsible is the liberal use of antibiotics before admission. A patient not infrequently has been treated as a follicular tonsillitis with penicillin for a few days until diphtheria is suspected, by which time the chances of obtaining a swab positive for diphtheria have become slender. The warning must, therefore, be repeated that the diagnosis must not depend upon the bacteriological report. A positive result will confirm, but its absence will not negate the diagnosis. The onus rests primarily on the clinician, but closer collaboration with the bacteriologist will achieve better results.

The Mortality Rate is shown in Table III. While in many other parts of the world the mortality rate has fallen to between 3-5%, it was 12.3% in this series. This is undoubtedly due to the delay in seeking medical attention. Particularly is this the case with admissions from the peri-urban areas. Of the 255 cases from outside

TABLE III. MORTALITY RATE ACCORDING TO AGE

Age (years)	Cases	Died	%
Under 1	72	13	18.1
1-3	199	34	17.1
3-5	246	39	15.9
5-7	191	23	12.0
7-11	223	26	11.2
11-16	98	4	4.1
16 and over	106	1	0.9
Total	1,135	140	12.3

Johannesburg 58 died, a mortality of 22.7%, while of 880 local cases 82 or 9.3% died. The mortality is shown separately for each age-group. It is highest in the youngest. There follows a steady decrement with each succeeding age-group until the age of 11 years, when the decline is sharp. Only one adult succumbed (a woman), of toxic myocarditis 8 days after admission.

Time of Death. Exactly half the deaths, 70 out of 140, occurred within 48 hours of admission, and a further 64 (45.7%) between the 3rd and 14th days. No deaths took place later than that, until after the 35th day when 6 (4.3%) died.

Cause of Death. An acute toxic myocarditis accounted for 120 (85.7%) of the deaths, and an associated broncho-pneumonia for 9 deaths. Paralysis associated with a late carditis and broncho-pneumonia caused 6 deaths, laryngeal obstruction complicated by a broncho-

pneumonia or a toxic myocarditis 3 deaths, and miliary tuberculosis and gastro-enteritis 1 death each.

DIFFERENTIAL DIAGNOSIS

1. *Nasal Diphtheria*. Two cases of a non-specific rhinorrhoea were encountered. Other conditions to bear in mind are (a) congenital lues, (b) foreign body, and (c) trauma to the septum from constant nose-picking. (Occurring by itself, the condition is not serious and no deaths resulted, but it is a common source of infection.)

2. *Faucial Diphtheria*

(a) *Tonsillitis* (254 cases). This is the commonest error of diagnosis. In the event of any doubt, the case should be treated as diphtheria. The late Dr. Bayer used to teach that the mere reaching for a throat swab was sufficient indication for the administration of antitoxin.

(b) *Stomatitis, including Thrush*. Twenty-two cases were mistakenly admitted as diphtheria. The exudates of thrush are more linear, milky white in appearance, and more diffuse in their distribution in the oral cavity. A stomatitis is also more diffuse; it affects the gums, buccal mucosa and lips and is often associated with a glossitis.

(c) *Syphilitic lesions* accounted for 5 admissions. They were all tertiary—2 cases where the palate was undergoing perforation, 2 with secondarily infected congenital perforations, and 1 with syphilitic granuloma extending down to the vocal cords.

(d) *Tuberculous ulceration* was present in 5 cases, in one of which it was associated with a fiery red pharynx, resembling an acute streptococcal throat, and in the others with pseudo-membranous exudates. All had a high fever and the diagnosis was established radiologically and by sputum examination. All responded rapidly to streptomycin, although the pulmonary lesions require prolonged treatment.

(e) *Tuberculous cervical lymphadenitis* was mistaken for a bull neck in 1 case.

(f) A case with post-nasal drip with an exudate on the posterior pharyngeal wall posed a diagnostic problem until an E.N.T. consultant established the presence of carcinoma of the antrum.

3. *Laryngeal Diphtheria*

Secondary laryngeal diphtheria presents no diagnostic difficulties. The presence of membrane in the throat is almost conclusive. The diagnosis of a primary laryngeal diphtheria is not always easy.

(a) *Bacterial laryngitis or acute laryngo-tracheo-bronchitis* accounted for 64 cases, 8 of which required tracheotomy. It is usually accompanied by high fever and there may be some pharyngeal inflammation. Until proved otherwise, it should be treated as diphtheritic. The mortality for those undergoing tracheotomy is high, owing to the extension of the inflammatory process to the bronchi and bronchioles.

(b) *Broncho-pneumonia* (23 cases) was another common source of error, but unlike the laryngo-tracheitis, differentiation is possible and tracheotomy contra-

indicated. Dyspnoea, hoarseness, stridor and restlessness are signs shared with diphtheria but, in broncho-pneumonia, fever is usually higher, respiration is more rapid and shallow, and examination of the chest usually reveals bronchial breathing or crepitations.

(c) Laryngitis is frequently associated with measles (20 cases), and may occur before the appearance of the rash, in which event confusion with laryngeal diphtheria is possible. A laryngitis occurring during the convalescent stage of measles is not infrequently diphtheritic. The association is an accepted entity. There were 6 cases of measles and laryngeal diphtheria in this series. Tracheotomy may be required in either condition.

(d) *Miliary tuberculosis*. One case was admitted, the mechanism of the dyspnoea and chest recession being similar to that in broncho-pneumonia.

(e) A *mediastinal mass* (1 case), subsequently proved to be leukaemic, was found in a case referred to us as one of laryngeal obstruction.

(f) A *congenital heart lesion*, because of dyspnoea and cyanosis, also gained admission for a case as one of laryngeal diphtheria.

(g) A case with *massive atelectasis of the left lung*, due to an obstruction of the left main bronchus by a tumour, also presented with dyspnoea and stridor and produced a suspicion of diphtheria. The effect was similar to that of a foreign body, for which one must be on guard, although no cases were discovered in this series.

A retropharyngeal abscess may also produce stridor and be mistaken for laryngeal diphtheria.

LARYNGEAL DIPHTHERIA

Bayer,⁴ reviewing the European cases at the Johannesburg Fever Hospital 1930-37, found 1,291 cases of diphtheria, of which 242 (18.7%) were laryngeal and 124 required tracheotomy. In the present series there were 112 cases of laryngeal diphtheria (9.9%), a considerably lower percentage, but the proportion requiring tracheotomy was slightly higher (69 cases—61.6% as against 51.2%). Of the 112, 20 were primary and 92 secondary laryngeal diphtheria.

The *Age Incidence and Mortality of Tracheotomy* is shown in Table IV. Four-fifths of the tracheotomies were performed on children under the age of 5 years. At ages above that, operation was not frequently required, and never over the age of 11. The mortality was 34.8%, which compares favourably with Bayer's

TABLE IV. TRACHEOTOMY CASES AND MORTALITY ACCORDING TO AGE

Age (years)	Cases	Died
Under 1	10	3
1-3	25	8
3-5	21	5
5-7	8	5
7-11	5	3
Total	69	24 (34.8%)

figure of 33.3%. Mortality did not appear to be influenced by the age of the patient. This is contrary to Bayer's assertion that 'in children under 1 year the outlook is usually hopeless'.⁴ Of 10 cases in this series

under the age of 1 year, 7 managed to survive. This may be due to the prevention and treatment of the complication of broncho-pneumonia by antibiotics, which were not yet discovered in 1937.

Of the 69 tracheotomies, 30 were performed on bull-neck diphtheria. In spite of the severity of their illness, almost half—14 cases—survived. Laryngeal obstruction must be relieved; extreme toxicity is no contra-indication for operation.

The operation favoured at Waterval Hospital is a low tracheotomy done under local anaesthetic.

COMPLICATIONS OF DIPHTHERIA

The toxins have a specific action on the heart, kidney, and nerve tissue, producing respectively a carditis, nephritis and neuritis.

Carditis

This was the most important complication. It probably occurs even more frequently than can be detected clinically or with an electrocardiograph.

Signs detected clinically were: tachycardia or bradycardia, extrasystoles, a weak first heart sound followed by splitting of the sounds, a systolic murmur, gallop rhythm.

E.C.G. changes were: slurring of the QRS complex, depressed S-T segments, inverted T waves, and bizarre pictures of conduction defects and bundle-branch block.

Prognosis. The majority of deaths were due to peripheral circulatory failure, associated with an acute toxic myocarditis. These deaths took place before the 14th day, but with the onset of paralytic complications there was a recurrence of signs (late carditis).

A gallop rhythm is of prognostic significance. Of 25 cases in whom a gallop rhythm was recorded, 9 died early on of an acute toxic myocarditis, while 13 developed palatal or pharyngeal paralysis, of whom a further 3 died. Half the cases with a gallop rhythm therefore died, and only 3 of the survivors did not suffer further complications.

A marked bradycardia, due to heart block, where the rate dropped to below 60/min, was also usually fatal.

Congestive cardiac failure developed in 5 cases, the earliest 5 days after admission, the latest 37 days. There were 2 deaths, one on the 8th day, the other on the 40th, the latter following the onset of a pharyngeal paralysis. Digitalis was used in 3 cases, 2 of whom recovered. The death was in a case which emerged successfully from congestive cardiac failure occurring on the 18th day, only to suffer a relapse on the 40th day, coincident with pharyngeal paralysis. Digitalis is not indicated in the arrhythmias of diphtheria, but its judicious use in a case with progressive congestive cardiac failure is occasionally life saving.

Renal Complications

Albuminuria, the presenting feature of toxic nephritis, was found in 114 cases (10%). A number of cases died before a urine examination could be made. The presence of albuminuria is an indication of the severity of the illness. Forty-four (38.6%) of those with albuminuria died, and of the survivors a further 36 developed paraly-

sis, with 4 deaths amongst them. Only 1 out of every 3 cases with an albuminuria, therefore, escaped death or other severe complications.

Oliguria and anuria were usually due to peripheral circulatory failure, anuria invariably having a fatal termination.

Neuritis

Ocular and facial palsies were each only noted in 2 cases and in themselves were not serious. Palatal paralysis occurred in 70 cases, an incidence of 6.2%. Twenty went on to develop pharyngeal paralysis, 5 of whom progressed to respiratory paralysis. Three cases required an artificial respirator (iron lung), with 1 death. Of the 70 cases, 6 died (a mortality of only 8.6%), 5 of an associated broncho-pneumonia and toxic myocarditis, while the 6th contracted an acute miliary tuberculosis, which proved fatal.

Some of the cases with palatal, and all with pharyngeal paralysis had a generalized peripheral neuritis, the lower limbs being affected more than the upper. Though convalescence was protracted, recovery was invariably and complete (excluding, of course, the 6 deaths.)

Time of Onset. The earliest onset of a palatal paralysis was the 8th day after admission, and the latest the 50th. The average was the 34th day. Pharyngeal and respiratory paralysis occurred in quick succession.

Age Distribution. No case of paralysis occurred under the age of 1 year, and only 1 in an adult. It was the older children who were most commonly affected.

Bull Neck

This is being considered under a separate heading in order to assess the prognosis. There were 296 cases classified as bull-neck (26.1% of admissions) with 108 deaths, a mortality of 36.2%. Paralytic complications occurred in 55 cases (18.6%), including 5 who died. In summary, 1 in every 4 admissions was a bull-neck case. Of every 6 bull-neck cases, 2 died, 1 developed paralysis, and 3 suffered no further complications. For non-bull-neck cases of grade-3 severity the figures were slightly lower, the mortality rate being 28.3% and paralytic complications 13.2%.

TREATMENT OF DIPHTHERIA

Since the introduction of antitoxin no great strides have been made in the treatment of this preventable disease. The dose of antitoxin used varies from 40,000 to 120,000 units according to the severity of the disease, irrespective of the age of the patient. It is given in one dose and is only repeated if, on reassessment, it appears that the severity was originally under-estimated. Reactions to serum are very rarely encountered in the non-European. In this series, ACTH and penicillin were used as adjuncts, but one cannot say that the mortality was appreciably influenced. Their use is nevertheless recommended.

In 1952, vitamin B 12 was tried prophylactically in an attempt to reduce the number of paralytic complications, and therapeutically once paralysis had already developed. The results did not appear sufficiently encouraging to

warrant a large-scale trial, and its use was subsequently abandoned.

The arrival on the scene, however, of erythromycin has been an advance in the treatment of the persistently positive case or carrier. Penicillin, aureomycin and terramycin had only moderate success in eliminating the diphtheria bacillus. Blute⁵ reported the use of erythromycin in 3 acute cases and 1 carrier, with the immediate disappearance of the bacilli. Since June 1954 we have used it in 20 cases who had persistently positive swabs despite the use of other antibiotics. In every case negative swabs were returned in 24 hours and continued negative.*

PROGNOSIS

Once the toxin has become fixed to the cells, little can be done to influence the course of the disease, but by careful assessment the probable complications can be anticipated. On admission the case is classified according to severity. In grade 1, no complications need be expected. In grade 2, less than 1% will not proceed uneventfully (1 death, and 2 with paralysis out of 390 cases). In grade 3 the chances of a bull-neck case are only slightly graver than those of non-bull-neck cases. One-third of the cases will die, and of the survivors about one-quarter will develop further complications. If a gallop rhythm or an albuminuria are present, paralytic complications can be expected to follow. If the case survives the 14th day, it stands a good chance of recovery. The next danger period is in the 5th week, with the onset of a palatal paralysis, often heralded by a spike in temperature or a listless appearance in a child who has previously been cheerful and playful. Between the acute and paralytic phases the patient often appears quite well, but the prognosis must remain guarded. If palatal paralysis clears before the development of a pharyngeal

* Subsequently we have experienced 2 cases in whom there was a delay of 72 hours after using erythromycin.

paralysis, no further complications are likely to follow. If the patient survives, recovery is complete.

CONCLUSION

The tragedy is the large number of cases which made the writing of this article possible. In most other countries, the scourge of diphtheria has disappeared. In South Africa the battle scarcely seems to have begun. The answer is not in finding a better therapeutic agent; the answer is in prophylaxis. The weapon has been in our hands now for many years, but active immunization is still not practised on a sufficiently large scale. Smallpox has practically been eliminated through compulsory vaccination. Similar legislation is required to enforce immunization of all infants against diphtheria.

SUMMARY

1,135 cases of diphtheria in the non-European are presented, with a case mortality of 12.3%, decreasing with age. The differential diagnosis of each type of diphtheria, and the incidence and prognosis of the major complications, are discussed. Mention is made of the use of erythromycin in eliminating the diphtheria bacillus from a case or carrier. The high incidence of the disease is stressed, and a plea is made for legislation enforcing immunization.

Thanks are due to Dr. B. Gaylis, Medical Superintendent, for advice, and to Dr. J. W. Scott Millar, the Medical Officer of Health, Johannesburg, for permission to publish this article.

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