THE INCIDENCE AND CLINICAL CORRELATION OF TYPES OF *CORYNEBACTERIUM DIPHTHERIAE* AT ROMFORD, ESSEX

A SURVEY OF 400 CASES

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In 1931, Anderson, Happold, McLeod and Thomson published an account of three types of the *Corynebacterium diphtheriae*, named by them *gravis*, *mitis* and *intermedius*, occurring among the cases of diphtheria at Leeds, and also showed that a correlation existed between the type of organism and clinical severity. Subsequent investigations have been carried out in various parts of the country, viz. Menton *et al.* (1933) in Staffordshire, Wright and Rankin (1932) in Edinburgh, Leete, McLeod and Morrison (1932) in Hull, Robinson and Marshall (1934) in Manchester, Carter (1933) in Glasgow, while Christison (1934) and Schiff and Werber (1935) have recorded their observations on the types occurring in Berlin. A communication by Mair and Joe (1934) to the Society of Medical Officers of Health gave an indication of the types present in 192 cases of diphtheria in London.

The present paper deals with an investigation into the incidence of types of the *C. diphtheriae* occurring in 400 consecutive cases of diphtheria admitted to the Romford Isolation Hospital during the period November 1934 to November 1935, from the surrounding Urban Districts of Dagenham, Hornchurch and Romford, whose combined population is approximately 230,000. In all three districts, but particularly in Dagenham, there has been a phenomenal growth in population during the past few years, and this growth is still proceeding, but at a slower pace. The child population is relatively high, and the period covered by the cases under review has been marked by a high incidence of a severe type of diphtheria. Thus the cases admitted to hospital in 1932 and 1933 totalled 278 with a case mortality of 6·0 per cent., compared with 1000 cases in 1934 and 1935 and a case mortality of 9·4 per cent. In common with many other places at home and on the Continent the incidence of laryngeal diphtheria has been remarkably low, forming about 2 per cent. of the total cases.

As is well known, many cases notified as diphtheria are found to be suffering from some other infection, and this paper excludes all those in whom the original diagnosis was not confirmed. The remaining 400 cases cover every range of clinical severity.

Treatment has been completed in all the cases.

CLINICAL CLASSIFICATION

A provisional estimate of clinical severity was made on admission for the purpose of treatment, and this estimate was later reviewed in the light of subsequent progress. Classification was as follows:

(1) Faucial diphtheria, mild, moderate, severe and haemorrhagic.
(2) Laryngeal (including laryngo-faucial) diphtheria.
(3) Nasal diphtheria.
(4) Carriers (or bacteriological cases).

LABORATORY PROCEDURE

Swabs from the nose and throat were taken from the patient on the day of admission and inoculated upon a Loeffler slope and a tellurite plate prepared according to the method of McLeod (see Anderson *et al.* 1931). The subsequent growth in broth, change in reaction in broth, and the fermentation reactions for glucose, saccharose, and starch were also recorded. The same procedure was also carried out with all doubtful or atypical colonies. Finally, the haemolytic power of all strains was determined by Hammerschmidt's method.

Little difficulty was experienced in classifying most strains as *gravis*, *mitis* or *intermedius*, types and this was especially noticed when cases of diphtheria were most prevalent and most severe.

TREATMENT

Antitoxin dosage

The aim in the administration of antitoxin was to give sufficient in one dose within an hour of admission. If a second dose was considered advisable, it was given within 12 hours of the first in amount equal to or greater than the original dose. For mild and moderately severe cases, antitoxin was given intramuscularly into the vastus externus, while severe and haemorrhagic cases received the greater part intravenously. The effectiveness of the dose was judged by the fall of temperature, the cessation of spread of the membrane, with the appearance of a definite edge, and the lessening of the adenitis. In a few cases, antitoxin appeared to have little effect, and large amounts of antitoxin, even intravenously, seemed to have no influence upon the course of the disease.

All cases were kept recumbent for 4 weeks before being allowed to sit up. If uncomplicated they were ambulatory in the sixth week. If paralysis or cardiac complications supervened, a further period of recumbency was given until these had disappeared. Cardiac stimulants were administered when necessary by intramuscular injection.

It is possible that an under-estimation of clinical severity at the time of admission and consequent under-treatment with antitoxin may result in

transforming a "mild" case into a "moderate" or even "severe" one. When, however, all mild cases, moderate cases, and severe cases were brought together and the dose of antitoxin examined and compared in each case, no great variation in dosage was found in the three clinical groups. Thus, the most frequent dose for a mild case was 20,000 units, for a moderate case 40,000 units, and a severe case 80,000–120,000 units. Very toxic cases received up to 200,000 units together with 50 per cent. glucose in saline intravenously.

Type incidence

Table I shows the number of cases of each type of *C. diphtheriae* occurring in 400 cases of diphtheria and their percentage distribution.

Table I

	Gravis	*Intermedius*	*Mitis*	Atypical	Mixed	Total
Cases	253	87	42	17	1	400
	63·2 %	21·7 %	10·5 %	4·2 %	0·25 %	

Table II shows for comparative purposes the percentage incidence of each type in different parts of the country.

Table II

Area	Year	*Gravis*	*Inter-medius*	*Mitis*	Atypical	Mixed
Leeds	1932	77·5	5·5	17·0	—	—
Hull	1933	59·4	29·0	8·7	2·3	0·5
Glasgow	1933	1·9	71·8	14·4	11·9	—
Manchester	1934	23·8	54·6	19·2	1·5	0·9
	1935	50·9	19·9	27·8	0·1	1·3
Liverpool	1935	37·2	45·8	17·0	—	—
Romford	1935	63·2	21·7	10·5	4·2	0·25

It will be seen that there is a great deal of variation in the incidence of the various types of *C. diphtheriae* in different parts of the country. In Manchester, Robinson and Marshall (1935) showed that there was a complete alternation of type in 1935 as compared with 1934. In the Romford area, the predominant type is gravis, although as will be shown later, it is not the most lethal.

Correlation of type with clinical classification

In Table III is shown the type of *C. diphtheriae* found in mild, moderate, severe and haemorrhagic faucial, laryngeal, nasal, and fatal cases in the 400 cases of this series.

The distribution of the *gravis*, *intermedius* and *mitis* types among cases of diphtheria from the Urban Districts of Dagenham, Hornchurch and Romford, correlated with clinical severity, is shown in Table IV.

Table III

	Gravis	*Intermedius*	*Mitis*	Atypical	Mixed	Total
Faucial diphtheria:						
Mild	116	44	21	11	1	193
Moderate	72	9	6	2	—	89
Severe	34	23	3	1	—	61
Haemorrhagic	12	6	—	—	—	18
Laryngeal	2	2	4	1	—	9
Nasal	13	3	8	1	—	25
Carriers	4	—	—	1	—	5
	253	87	42	17	1	400
Fatal cases	24	12	2	—	—	38

Notes. (1) In the atypical group, the morphological appearance of the colonies on tellurite medium was at variance with the cultural and biochemical reactions. In subsequent tables, they are included in the type they most resemble.

(2) The only example of mixed infection in the same patient was obtained from a mild faucial case, with a *gravis* infection in the nose and an *intermedius* infection in the throat.

Table IV

	Dagenham			Hornchurch			Romford			
	Gravis	*Inter-medius*	*Mitis*	*Gravis*	*Inter-medius*	*Mitis*	*Gravis*	*Inter-medius*	*Mitis*	Total
Faucial cases:										
Mild	53	28	13	26	7	7	45	9	5	193
Moderate	20	5	3	28	3	—	26	1	3	89
Severe	11	12	2	11	5	1	13	6	—	61
Haemorrhagic	3	4	—	4	1	—	5	1	—	18
Laryngeal	1	2	1	—	—	1	1	—	3	9
Nasal	7	3	6	2	—	—	5	—	2	25
Carriers	3	—	—	—	—	1	1	—	—	5
	98	54	25	71	16	10	96	17	13	400
Fatal cases	8	7	2	8	1	—	8	4	—	38

In Dagenham there was a much higher incidence of the *intermedius* type than in the other Urban Districts, which show an almost similar percentage distribution of type in the cases derived from those areas, thus:

Percentage distribution of types from the cases from the Urban Districts shown

	Gravis	*Intermedius*	*Mitis*
Dagenham	55·1	30·6	14·3
Hornchurch	73·8	15·7	10·5
Romford	76·0	13·6	10·4

FATAL CASES

The total number of deaths was thirty-eight or 9·5 per cent. An analysis of the fatalities is given in Table V:

Table V

	Gravis	*Intermedius*	*Mitis*	Total
Toxic	22	10	—	32
Paralytic	2	2	—	4
Obstructive	—	—	2	2
	24	12	2	38
Fatality rate	9·5	13·8	4·8	

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Of the thirty-two toxic deaths, eighteen were of the haemorrhagic type, distributed as follows:

Gravis	*Intermedius*	*Mitis*
12	6	—

It is evident that the *intermedius* type had the greatest lethal power in the present series of cases. In those infected with this type, the fatality rate was 13·8 per cent. as compared with a fatality rate of 9·5 per cent. in those infected with the *gravis* strain. There is also a much higher proportion of severe faucial cases in the intermediate group. If the severe faucial cases and the fatal toxic cases are combined and expressed as a percentage of the total cases for each type, the percentage due to *intermedius* is 31·0 per cent. as compared with 17·6 per cent. due to *gravis*, an indication of comparative severity.

Table VI shows the percentage incidence of albuminuria and paralysis in the three types:

Table VI

	Gravis	*Intermedius*	*Mitis*
Albuminuria	38·4	40·4	18·1
Paralysis	20·8	21·4	11·3

The two fatal cases due to *mitis* infection were severe laryngo-faucial cases with respiratory obstruction. Tracheotomy was performed in both cases with temporary relief, death being due to the combined effects of respiratory failure and toxaemia.

Laryngeal diphtheria

There were only nine cases (or 2·25 per cent.) in the present series. All three types, *gravis*, *intermedius* and *mitis*, were represented, but the *mitis* type was the most common.

Day of disease

A factor of great importance as regards subsequent progress is the period of time which elapses between the onset of the disease and the commencement of treatment, in other words, the day of disease on admission to hospital. It appeared worth while to tabulate the day of disease for each type as shown in Table VII.

Table VII

Day of disease	*Gravis* cases	*Intermedius* cases	*Mitis* cases
1st	21 (1)	6 (1)	2
2nd	73 (5)	32 (5)	8
3rd	64 (5)	25 (4)	8
4th	47 (9)	11 (2)	7
5th	29 (2)	7	5 (1)
6th	10 (1)	2	5
7th	4	—	1 (1)
8th	3 (1)	—	1
Later	13	5	11
	264 (24)	88 (12)	48 (2)

Figures in parentheses denote number of deaths.

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It will be seen that the majority of *gravis* and *intermedius* cases came under treatment at an early date, the greatest number on the second day. With *mitis* cases there was a slight delay of approximately 24 hours, an indication that the clinical manifestations of this type are less evident in the early stage. Faucial cases of this type are usually mild, but there were two fatal cases in this group as mentioned above.

The table also supplies further evidence of the greater severity of *intermedius* infection. With *gravis* cases, the fatality rate, according to the day of disease, increased with the delay in admission to hospital, whereas with *intermedius* cases, the fatality rates remain fairly constant throughout, thus:

Day of disease	Fatality rate	
	Gravis	*Intermedius*
1st	5·2	16·6
2nd	7·0	15·6
3rd	8·0	16·0
4th	19·9	18·1
5th	7·0	—
6th	10·0	—

AGE OF PATIENT

During the course of the investigation, it was a matter of common observation that older children were as readily attacked as the younger and presumably more susceptible ones. Table VIII gives the number of cases at each age for each of the three types of *C. diphtheriae*:

Table VIII

Age in years	*Gravis*	*Intermedius*	*Mitis*
1	2	2	1 (1)
2	7	—	1
3	11 (2)	4 (2)	2
4	18 (3)	13 (2)	6
5	28 (4)	7	11 (1)
6	40 (2)	12 (3)	2
7	33 (3)	6	3
8	31 (3)	6	5
9	21 (2)	5 (2)	4
10	16 (1)	5	3
11	16 (3)	6 (3)	1
12	10	5	2
13	7 (1)	2	1
14	3	3	2
15	2	2	1
Over 15	19	10	3
	264 (24)	88 (12)	48 (2)

Figures in parentheses denote fatal cases.

With both *gravis* and *intermedius* cases, almost 60 per cent. are 7 years of age or older. In the case of *mitis*, the percentage is lower with most cases at 5 years of age.

SUMMARY

1. A consecutive series of 400 cases of diphtheria from the Romford (Essex) area have been bacteriologically typed and correlated with the clinical findings.

2. *Gravis* infection was found to be the most prevalent type.

3. The *intermedius* type was the most lethal and severe.

4. *Mitis* infection formed the smallest proportion of cases, usually of a mild character.

5. Laryngeal cases were few, and all three bacteriological types were represented.

6. A large proportion of children of 7 years and over were attacked.

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REFERENCES

ANDERSON, HAPPOLD, MCLEOD and THOMSON (1931). *J. Path. and Bact.* **34**, 667.
CARTER, H. S. (1933). *J. Hygiene*, **33**, 542.
CHRISTISON, M. H. (1934). *Ztrbl. f. Bakt.* Abt. I, **133**, 59.
LEETE, MCLEOD and MORRISON (1932). *Lancet*, ii, 1141.
MAIR and JOE (1934). *Ibid.* i, 299.
MENTON, COOPER, DUKE and FUSSELL (1933). *J. Hygiene*, **33**, 414.
ROBINSON and MARSHALL (1934). *J. Path. and Bact.* **38**, 73.
—— —— (1935). *Lancet*, ii, 441.
SCHIFF and WERBER (1935). *Deutsche med. Woch.* **61**, 259.
WRIGHT and RANKIN (1932). *Lancet*, ii, 884.

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