Observations on the diagnosis of diphtheria : combined bacteriological and clinical evidence / by F. Foord Caiger and R.A. O'Brien.

Contributors

Caiger, F. Foord.
O'Brien, Richard Alfred, 1878-1970.
Wellcome Physiological Research Laboratories.

Publication/Creation

[Place of publication not identified] : [publisher not identified], [1924?]

Persistent URL

https://wellcomecollection.org/works/vurm5pfz

wellcome collection

Wellcome Collection
183 Euston Road
London NW1 2BE UK
T +44 (0)20 7611 8722
E library@wellcomecollection.org
https://wellcomecollection.org

133

P. 4358
133

OBSERVATIONS

ON THE

DIAGNOSIS OF DIPHTHERIA

Combined Bacteriological and Clinical Evidence

BY

F. FOORD CAIGER, M.D., F.R.C.P.Lond.,

CHIEF MEDICAL OFFICER, INFECTIONS HOSPITAL SERVICE, M.A.B.;

AND

R. A. O'BRIEN, C.B.E., M.D. Melb., D.P.H.,

DIRECTOR OF THE WELLCOME PHYSIOLOGICAL RESEARCH LABORATORIES.

Reprinted from The Lancet, *July 12th*, 1924, *p.* 53.

Digitized by the Internet Archive
in 2018 with funding from
Wellcome Library

https://archive.org/details/b30624435

THE

DIAGNOSIS OF DIPHTHERIA:

COMBINED BACTERIOLOGICAL AND CLINICAL EVIDENCE.

THE investigation described in this paper was made in order to see if laboratory methods, applied as thoroughly as possible to every case admitted with a diagnosis of diphtheria into an infectious fever hospital, would be helpful. In other words, would the extra time and trouble involved in such work give any real help (*a*) in the interests of the patient, (*b*) in the interests of hospital administration?

Procedure.

The patients were admitted to the South-Western Hospital of the Metropolitan Asylums Board. From every patient admitted with a diagnosis of diphtheria a swab was taken in the receiving-room by the medical officer on duty, and a clinical diagnosis made by her and entered in the record as "diphtheria," "probably diphtheria," "not diphtheria," or "probably not diphtheria." The first two groups are considered as a positive admission-room diagnosis of diphtheria, and appear in Table I. as *b*+; the two latter are recorded as a negative admission-room diagnosis, and appear as *b*−. The swab was sent to the Wellcome Physiological Research Laboratories some six miles away, where it was usually received the same day, and sown on Löffler's medium. From the swab a "direct smear" was made, and stained by Gram's method, in order to detect Vincent's organisms or streptococci, if present. After incubation for 18 to 24 hours a smear was made from the culture, and if organisms morphologically indistinguishable from K.L.B. were found, the laboratory diagnosis was entered as "M.D.B." Throughout this paper "M.D.B." is used to indicate bacilli morphologically indistinguishable from the *Bacillus diphtheriæ;* this is essentially a microscopic diagnosis. "K.L.B." is used to indicate a bacillus which microscopically appears to be *B. diphtheriæ*, isolated in pure culture, which ferments glucose but not saccharose, and may be virulent or avirulent to guinea-pigs.

The culture made from the swab on Löffler's medium and allowed to grow overnight was in most cases injected intradermically into guinea-pigs. From the swab or the culture on Löffler's medium plates were always sown, and one or more colonies picked off, grown for 24 hours, and injected intradermically

into guinea-pigs.[1] In special cases the subcutaneous method was also used. If the provisional diagnosis made did not agree with the clinical diagnosis, a second swab was asked for. Thus the clinical and laboratory workers each had, while the patient was available, the opportunity of reviewing the diagnosis in view of the other's evidence.

The clinical work fell mainly on Dr. Amy Thoms and Dr. Ruby Inkster; the laboratory work was carried out by Dr. A. J. Eagleton (in the earlier part of the series), and Dr. C. C. Okell, Dr. H. J. Parish, and Miss M. Baxter throughout. From time to time the results were reviewed in conference by the above workers together with ourselves. Since the whole problem was approached from the clinical standpoint, the final decision in all cases rested with the clinician.

Results.

The investigation was carried on until 700 swabs had been examined. They are divided into two series, G, 1 to 600, and A, 1 to 100; 520 patients in all were examined. In Table I. are given the general results. If we consider for the moment series G, 1 to 600, it will be noted that in the case of 58·3 per cent.—i.e., cols. B, F, G, and D—of all patients certified before admission as "bacteriological" or "clinical" diphtheria, the diagnosis was confirmed,

TABLE I.—*Showing the General Results of the Examination.*

—	A	B	C	D	E	F	G	H
	Cases	Agreements—		*a* + *b* − *c* −	*a* − *b* + *c* −	*a* + *b* − *c* +	*a* − *b* + *c* +	*a* − *b* + *c* ?
		+	−					
G. 1–100	70	45	12	—	12	—	1	—
101–236	106	41	32	5	22	2	4	—
237–456	162	78	34	3	32	11	4	—
457–600	98	47	28	1	10	10	2	—
Total .	436	211 (48·4)	106 (24·3)	9 (2·1)	76 (17·4)	23 (5·3)	11 (2·5)	—
A. 1–100	93	57 (61)	15 (16)	1 (1)	2 (2)	—	10 (11)	8 (9)

a, Laboratory diagnosis. *b*, Admission-room diagnosis. *c*, Final clinical diagnosis.

while in 41·7 per cent.—i.e., cols. C and E—the original diagnosis could not be confirmed either clinically or bacteriologically. It is not suggested that this whole group represents definite errors in clinical diagnosis made by outside practitioners. Some of these "negative" patients had probably

[1] Eagleton and Baxter: Brit. Med. Jour., 1921, i., 775.

had clinical diphtheria a few days previously, and were "clearing up" when admitted. We must also remember that the general practitioner or the medical officer in a general hospital is often faced with a situation in which he considers it justifiable to send the patient to a fever hospital as a precautionary measure or on grounds of expediency.

Col. D: From nine cases virulent bacilli were isolated when the "admission diagnosis" and the final clinical diagnosis were negative. These would seem to be patients who had yielded a "positive" result during the swabbing of contacts or routine swabbing of schools or families. All nine carriers within a few weeks gave a succession of negative swabs. It is worthy of remark that col. D—i.e., the "carriers"—represents only 2 per cent. of the total admissions. We anticipated that most of the cases considered clinically negative by the hospital staff would have fallen into this group, whereas they fall into the group in which both the bacteriological and clinical evidence failed to confirm the diagnosis made before admission.

Col. E: Here the laboratory worker failed to find bacilli in one or more swabs and the clinician made the final diagnosis negative, though on admission the condition of the patient had justified a provisional clinical diagnosis of "probably diphtheria."

Col. G: These 11 cases are of considerable interest; in Table II. are given details.

TABLE II.—*Clinical Diagnosis Positive, but Laboratory Diagnosis Negative in all 11 Cases.*

	No. of cases.
Two negative swabs	1
Three ,, ,, ...	4
Four or more negative swabs	2
Very few M.D.B.: not isolated	2
Avirulent (several colonies examined) ..	2

The notes from these cases have subsequently been carefully considered in conference; the laboratory workers' evidence in all these instances—i.e., the examination by cultural and inoculation tests—have failed to yield the results which are regularly obtained in frank clinical diphtheria. The clinicians, on the other hand, on reviewing the clinical records, felt that the course of the illness so closely resembled frank clinical diphtheria that a diagnosis of diphtheria was the only one open to them.

The only point of outstanding interest is that in several of these instances the patient was admitted late in the course of a severe attack and received serum at a late stage of the disease; one would have expected some paralytic or myocardial symptoms to appear during convalescence, but this expectation was not realised and in none did these symptoms

appear. More than one of these patients was shown to a class of students and a prognosis of paralysis during convalescence made, but no paralysis developed. Clinically, these cases certainly did not resemble syphilitic pharyngitis. It may be that the illness in these patients was caused by Vincent's organisms or streptococci. We are of the opinion that few, if any, of these cases can be thus explained, for we were naturally alive to these possibilities and had examined direct smears in every case.

From two patients avirulent organisms only were isolated. When the result of the virulence test was known some days had elapsed, and the opportunity of getting a second swab at an early stage of the disease had disappeared. The facts relating to these two patients are recorded above; virulent organisms may have also been present in the throat, but the swab either failed to collect any virulent organisms or collected extremely few, which could not be isolated. The few investigations that have been made indicate that probably more than 1 per cent. of the general population in London carry avirulent K.L.B. in their throats. Among 554 patients sent into a hospital one would expect to find a small number carrying avirulent K.L.B., in addition to the causal virulent organisms. The laboratory workers have found, in a total of approximately 2000 examinations in the past few years, three instances of the association of virulent and avirulent K.L.B. in the same culture, one from a healthy carrier, one from a convalescent patient, and one from a case of diphtheria.

The examinations in series A, 1 to 100, were carried out before those in series G, and before the arrangements for rapid interchange of results were working as smoothly as during the later G series. The general results resemble those of series G, except that under cols. G and H 20 per cent. of the patients appear, whereas in series G col. H is unnecessary, and col. G contains only 2·5 per cent. Without emphasising the point too far, we are inclined to believe that, as the general result of this earlier work, the clinician came to feel that the laboratory evidence gave definite aid, and that where the "admission diagnosis" and the laboratory diagnosis did not agree there was a gradually increasing tendency to revise the "admission diagnosis." The results obtained from series A are not represented in the percentages quoted throughout the paper and in the general discussion.

The following points of interest emerged during the inquiry:—

1. In 95·5 per cent. of cases in which the diagnosis of diphtheria was confirmed, the first swab sent to the laboratory was found to be positive, and it is

worthy of note that by the technique adopted virulent *B. diphtheriæ* were isolated from 93·5 per cent. (Table III.).

TABLE III.—*Clinical Diagnosis Positive in 245 Cases.*

	Cases.		Percentage.	
First swab positive—				
K.L.B. isolated—Virulent ..	229	234	93·5	95·5
,, ,, —Avirulent ..	2		0·8	
Very few M.D.B. present, not isolated	3		1·2	
Swab negative	11		4·5	

2. In five cases in a total of 436—i.e., 1·15 per cent. —later examination changed a negative laboratory diagnosis, which had been based on the examination of the first swab, into a positive diagnosis.

3. Amongst 234 patients where the clinical diagnosis was positive and M.D.B. were seen in the smear, isolation of virulent organisms was successful from the first swab in 231 instances, while in three instances —i.e., 1·2 per cent.—M.D.B. were seen in the first swab but could not be isolated, whereas from a second swab virulent K.L.B. were obtained.

4. Three laryngeal cases occurred in the series; from one virulent K.L.B. were obtained; from two, with a clinical diagnosis "uncertain, ? laryngeal diphtheria," no M.D.B. were obtained in culture.

5. In only two instances the clinical diagnosis was "nasal diphtheria," but from neither were K.L.B. obtained.

6. Amongst 182 cases clinically negative, no M.D.B. were obtained from cultures in 167 instances—i.e., 91·7 per cent.; in 11 instances—i.e., 6 per cent.— very few M.D.B. were seen in the smear made from an overnight culture, but could not be isolated. It is probable that none of these were true K.L.B.

From four only avirulent K.L.B. were isolated. From the cultures obtained from each of these four patients a number of colonies were examined for virulence.

Summary of Results.

1. Approximately 529 patients certified as suffering from diphtheria and admitted to the South-Western Hospital were included in the examination; 436 of them were closely studied. In 59 per cent. the diagnosis of diphtheria was confirmed. In 41 per cent. the diagnosis could not be confirmed.

2. Only nine cases, or approximately 2 per cent. of the whole, were healthy "carriers" of virulent *B. diphtheriæ*.

3. The laboratory workers' diagnosis agreed with the clinical diagnosis in 97·5 per cent. of instances;

in 11 cases (2·5 per cent.) the laboratory evidence was directly against a diagnosis of diphtheria, while the clinical evidence was quite definitely in favour. No completely satisfactory explanation of these discrepancies suggests itself.

4. The first swab examination at the laboratory was found to be positive in 95·5 per cent. of instances in which the diagnosis of diphtheria was confirmed. From 93·5 per cent. virulent diphtheria organisms were isolated. In only 1·15 per cent. was a negative diagnosis which had been made from the first swab changed into a positive diagnosis by the examination of later swabs.

5. Two cases only were diagnosed as "nasal diphtheria," but from neither were *B. diphtheriæ* isolated.

Conclusions.

With regard to the questions set forth at the beginning of the inquiry we can answer:—

1. There is no evidence that the information obtained by the inquiry has altered or improved the prognosis or treatment of the patients suffering from diphtheria.

2. From the administrative point of view the inquiry has been justified; we feel that the investigation has resulted in an increased confidence and accuracy of diagnosis amongst the clinicians taking part. It should therefore facilitate the allocation of patients to the different wards in the hospital and ensure their release in "negative" cases at an earlier date than would be justifiable without full coöperation with the laboratory worker.

3. The accuracy of hospital statistics is much improved by the coöperation of the laboratory worker.

4. From the point of view of accuracy of diagnosis, we are definitely of opinion that laboratory facilities similar to those described should be available in all large hospitals for infectious fevers.

The amount of laboratory work was very large, and it is probable that after this preliminary careful exploration of the field information of similar value can continuously be supplied by the laboratory worker, even if he dispenses with the routine animal tests and trusts to isolation and fermentation tests of pure colonies. The true *B. diphtheriæ* invariably and rapidly ferments glucose, but never saccharose. The animal test should be available in doubtful or difficult cases.

The Lancet Office,
1, Bedford Street, Strand, W.C.2