THE PRINCIPLES AND PRACTICE OF DIPHTHERIA IMMUNIZATION

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BY

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THE PRINCIPLES AND PRACTICE OF DIPHTHERIA IMMUNIZATION

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TO

MY FIRST TEACHER

JOHN DAVIES

IN HIS NINETIETH YEAR

FOREWORD

By OSCAR M. HOLDEN, M.D., D.P.H.

I AM very happy, and indeed honoured, to write a brief foreword to introduce Dr. Tudor Lewis's monograph. The patient investigation and painstaking recording which have gone into its compilation are sufficient guarantee for the soundness of the arguments put forward and the conclusions arrived at.

Amidst the mass of literature dealing with diphtheria immunization, there is a need for a short authoritative publication which, not pretending to go exhaustively into the subject, is sufficiently detailed to satisfy the scientific and inquiring mind; whilst, at the same time, providing guidance to the man who desires to carry out immunization upon sound lines, but has no wish to delve into the mysteries of serum chemotherapy. Dr. Lewis's book meets these two demands admirably.

It is peculiarly fitting that it should be published now, when great numbers of susceptibles are living under abnormal conditions and when diphtheria of the gravis type is showing evidences of epidemic prevalence. The influx of children into rural areas which are relatively 'unsalted' and the indiscriminate crowding together of masses of the population in air raid shelters will, unless a miracle happens, lead to grave dangers, among which diphtheria takes a prominent place.

In this country much is left to the decision of the individual. This would be excellent policy if all individuals had good reasoning faculties and had been trained to use them aright. Unfortunately, such a state of social perfection has not yet been attained. In the meanwhile the medical profession and, by no means least, the general medical practitioners have a responsibility in the general efforts to prevent diphtheria. Who can bring about the education of the parent in the proved value of immunization better than the trusted family doctor? I commend this small but concise and valuable book

to their careful perusal. They will then be fully armed to answer questions and to overcome criticism.

For the whole-time workers in public health medicine, this book will provide them with up-to-date arguments for and against various methods which have, from time to time, been put forward and will enable them to draw their own deductions. It will also provide them with valuable facts with which to influence those who have the shaping and education of the great proportion of the school children of this country. The influence of head teachers upon parents in promoting acceptance of immunization is very considerable, and in any scheme of propaganda this interest and help should always be elicited.

With every confidence I predict a very useful future for this publication and I venture to congratulate Dr. Lewis upon compiling so readable and concise an exposition of the principles of diphtheria immunization.

OSCAR M. HOLDEN.

January 1941

PREFACE

THE work described in the following pages was planned and conducted at the behest and under the supervision of my chief, Dr. Oscar M. Holden, Medical Officer of Health for Croydon, whom I sincerely thank for giving me the opportunity of undertaking it and for permitting me to publish it in its present form. Although fully engaged in the multifarious duties of a large public health department, and with the added responsibility of organizing and controlling the Casualty and Ambulance sections of the A.R.P. Service, he has always found time to read, criticize, and pronounce upon whatever I placed before him; and I am accordingly very grateful. I am grateful, too, to Dr. D. D. Payne, M.O.H. for Harrogate, and sometime deputy M.O.H. for Croydon, for much valuable help and advice, and to my colleague Dr. Edward Harte who has made many practical suggestions.

I have had the privilege and good fortune to be able to consult with the two foremost authorities in this field—Dr. H. J. Parish and Mr. A. T. Glenny of the Wellcome Physiological Research Laboratories. The unique experience of these two workers was placed unstintingly at my disposal and has been an inestimable advantage. In addition to giving me much information and constructive criticism, Mr. Glenny arranged for the blood antitoxin titrations on my cases to be carried out in his laboratory, and very kindly contributed the note on page 30. But I am especially indebted to Dr. Parish, who at a very difficult period and often at short notice has always been able to find time to help me out of difficulties. It is impossible to thank these two authorities sufficiently, for without their help and guidance this work could not have been carried out. My best thanks are also due to Sir Wilson Jameson, Dean of the London School of Hygiene, for his encouragement and many kindnesses, and for permission to use the library of the School; and to Dr. Bradford Hill, also of the School of Hygiene, for advising on the statistical

sections. Miss L. F. Wybrew, the health visitor in charge of diphtheria immunization in Croydon, has been uncomplaining in spite of extra work and has rendered great assistance in filing cards and making appointments, &c.

To compile an exhaustive bibliography of the work done on this subject would be a truly monumental task and so the list of references given is by no means complete. I have tried, rather, to pick out the work that has seemed to me to be of real and obvious importance, and this has meant omitting much that is of great interest and value but perhaps merely descriptive, repetitive, or otherwise inconclusive. To the authors of such papers I apologize, but a complete list would require several volumes. Some of the observations quoted have already been recorded in the *British Medical Journal*, the *Medical Officer*, and *Public Health* and I am grateful to the Editors of these journals for their permission to include them here in somewhat altered guise.

Originally the investigations were planned to decide the best methods for use in this town, as a prelude to extensive immunization, and were conceived on a larger scale. It was intended, for instance, to obtain a very much larger series of blood antitoxin estimations and ultimately to demonstrate the effect on diphtheria incidence of properly conducted immunization. This was not to be, for the extra duties imposed by the war made a continuance of the research impossible. In many ways, therefore, the work is incomplete. But if it is incomplete I do not think it is inconclusive, for I am perfectly satisfied that the methods advocated are the ones best suited for routine purposes. When so many children in the large towns are passing their nights in subterranean congestion, and the rural areas are receiving large numbers of potential carriers, it is surely the time for this powerful weapon to be fully utilized. Perhaps this small volume will do something to dispel doubts and indicate the best method of attack.

J. T. L.

January 1941

GLOSSARY OF TERMS AND ABBREVIATIONS USED IN THE TEXT

Antigen. A substance which when introduced parenterally into the tissues of an animal stimulates the production of an antibody.

Antibody. A substance that appears in the blood-stream of an animal in response to the parenteral introduction of an antigen. In the case of the diphtheria antigens the antibody is diphtheria antitoxin.

Unit of Antitoxin. That amount of antitoxin that has the same combining power as one unit of the standard antitoxin, which is equivalent to that amount of antitoxin that will completely neutralize 100 minimal lethal doses of toxin [one minimal lethal dose of toxin is the smallest amount of toxin that will kill a 250 grm. guinea pig within 4 days after subcutaneous injection].

Titre. A general term used to denote the quantity of antitoxin or antibody that appears in the blood of an animal in response to the introduction of an antigen.

Priming Injection or Primary Injection. The initial injection of a diphtheria antigen into an animal with little or no previous experience of diphtheria toxin.

'*Primed*'. The state of an animal which has received a primary injection and is able and ready to give a rapid antitoxic response to a secondary injection.

Secondary Injection. An injection of an antigen into an animal which is primed to produce antitoxin.

A.P.T. Alum precipitated toxoid.

F.T. Formol toxoid.

T.A.F. Toxoid-antitoxin floccules.

T.A.M. Toxoid-antitoxin mixture.

T.A.T. Toxin-antitoxin mixture.

A.U. Antitoxic unit.

C.C. Cubic centimetre.

Lf. The Lf. dose of toxin is that amount of toxin which when mixed with one unit of antitoxin gives optimal flocculation.

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CHAPTER I

THE PRESENT POSITION—THE NEED FOR A GENERAL STANDARD

FIFTY years ago Simon (1890) wrote, 'as exact knowledge is gained of agencies prejudicial to the public health the nation will provide against them; but for obvious reasons it is not likely that practical reforms will keep abreast of scientific progress'. Few prophecies can have had so unfortunate a fulfilment, in at least one branch of medical science. More than twenty-five years have elapsed since active immunization against diphtheria was introduced by Von Behring; its value has now been proved beyond doubt, but still its practical application, in this country, lags sadly behind. In no commercial undertaking could such a state of things exist, and it would be a spectacle not without a certain humour, were it possible to trifle with the thought each year of 3,000 preventable deaths. Much has been written, and more spoken, on the reason for our failure, and it has become a platitude to bewail the apathy of the public and to condemn its inertia. A recent leading article (*Lancet*, 1940) is more honest. 'Of all failures', says the writer, 'in our National Health policy the most unforgivable is our inability to bring down the high incidence of diphtheria in children—it is difficult to avoid the conclusion that the public fail to seek immunization principally because they are ignorant of its benefits and that some at least of the blame must be put on a lack of conviction within the medical profession.' This seems a just sentence. It is impossible for the medical profession generally and the public health service in particular, both central and local, to consider itself absolved of responsibility.

While the profession may not shirk liability for its own shortcomings it is not difficult to understand how they have arisen. And with understanding comes mitigation. The Chief Medical Officer to the Ministry of Health in his report for

1937 hinted at one of the reasons when he said: 'it is probable that the lack of a general standard has militated against the more general adoption of anti-diphtheria immunization in this country.' The profession has been, in other words, a camp of many councils. Some authorities recommend this prophylactic, others favour that, and many conflicting reports have appeared in the journals. Some say the Schick test should always be carried out, others that it has no practical value. The result has been that general practitioners and medical officers of health have been bewildered to know what method to adopt, and a reticence to advocate it vigorously has been the consequence.

To obtain the views of medical officers of health on this subject a questionnaire was sent by Dr. O. M. Holden, Medical Officer of Health for Croydon, to all the County Boroughs, all the Municipal Boroughs and Urban Districts in England and Wales with a child population of over 5,000, and to all the Metropolitan Boroughs. The results are shown in Table I.

TABLE I. *Analysis of results of questionnaire on methods used in immunization schemes*

Number of forms sent out	146
Number of replies received	144
Number of areas with no organized immunization scheme	10
Number of areas with no organized scheme, but with facilities available for immunization if required	4
Number of schemes from which the following data are taken	130

The use of the Schick Test.	*Total*	*Per cent.*
A Primary Schick and a Final Schick on all cases	8	6·2
A Primary Schick on all cases over 5 years and a Final Schick on all cases	19	14·6
A Primary Schick on a proportion of cases and a Final Schick on all cases	25	19·2
No Primary Schick but a Final Schick on all cases	18	13·8
A Primary Schick on a proportion of cases and a Final Schick on a proportion of cases	7	5·4
No Primary Schick but a Final Schick on a proportion of cases	6	4·6
A Primary Schick on a proportion of cases with no Final Schick	6	4·6
No Primary Schick and no Final Schick	41	31·5

*Materials and methods employed.	Total	Per cent.
Formol toxoid only	1	..
Toxoid-antitoxin mixture only	18	13·8
Toxoid-antitoxin floccules only	41	31·5
Alum precipitated toxoid by two injections only	25	19·2
Alum precipitated toxoid by one injection only	1	..
Alum precipitated toxoid by two injections in children over 5 years / Alum precipitated toxoid by one injection in children under 5 years	1	..
Alum precipitated toxoid by two injections and one injection with no stated discrimination	1	..
Alum precipitated toxoid by three injections	2	..
Formol toxoid and alum precipitated toxoid by two injections	1	..
Formol toxoid and alum precipitated toxoid by one injection	1	..
Formol toxoid and toxoid antitoxin floccules	2	1·5
Toxoid-antitoxin mixture and toxoid antitoxin floccules	8	6·2
Toxoid-antitoxin floccules and alum precipitated toxoid	22	16·9
Toxoid-antitoxin mixture and alum precipitated toxoid	5	3·8
All preparations as advised by medical officer	1	..

Immunization performed mainly in:	Total	Per cent.
Elementary Schools only	5	3
Infant Welfare Centres only	12	9
Separately organized clinics only	46	35
Elementary Schools and Infant Welfare Centres	21	16
,, ,, ,, Separate Clinics	13	10
,, ,, ,, Infant Welfare Centres and Clinics	14	11
Infant Welfare Centres and Clinics	13	10
Mainly by general practitioner	6	5
†Partly but not mainly by general practitioner	27	21

‡*Methods of propaganda.*	Total	Per cent.
Talks at Welfare Centres and School inspections	77	59
Distribution of leaflets	108	83
Posters in the town	44	34
Birthday cards or letters	18	14
Talks at parents' organizations	4	3
Film shows at parents' meetings	14	11
Local Press	8	6
Letters on School entry	2	1
Circular letters.	7	5
Overprinting of departmental envelopes	1	..
Talks with head teachers	1	..
No propaganda	1	..