POLYMYOSITIS

BY

JOHN N. WALTON

M.D., M.R.C.P.

First Assistant in Neurology, King's College, University of Durham, in the Royal Victoria Infirmary, Newcastle upon Tyne

AND

RAYMOND D. ADAMS

M.D.

Bullard Professor of Neuropathology, Harvard University

E. & S. LIVINGSTONE LTD.

EDINBURGH AND LONDON

POLYMYOSITIS

BY

JOHN N. WALTON

M.D., M.R.C.P.

First Assistant in Neurology, King's College, University of Durham, in the Royal Victoria Infirmary, Newcastle upon Tyne. Late Nuffield Foundation Fellow in Neurology and Neuropathology, Harvard Medical School and Massachusetts General Hospital, Boston, Mass., and King's College Travelling Fellow in the Neurological Research Unit, the National Hospital, Queen Square

AND

RAYMOND D. ADAMS

M.D.

Bullard Professor of Neuropathology, Harvard University and Chief of the Neurological Service, Massachusetts General Hospital, Boston, Mass.

E. & S. LIVINGSTONE LTD
EDINBURGH AND LONDON
1958

POLYMYOSITIS

PRINTED IN GREAT BRITAIN

PREFACE

THE unique position of progressive muscular dystrophy as the prototype of a primary disorder of muscle has been challenged in recent years by a number of new diseases. These have been introduced to the medical profession under a variety of terms such as dermatomyositis, polymyositis, neuromyositis, paroxysmal and sporadic myohæmoglobinuria, interstitial polymyositis with 'collagen' diseases (rheumatoid arthritis, disseminated lupus erythematosus and scleroderma), generalised myositis fibrosa, generalised myositis ossificans, calcinosis universalis, menopausal muscular dystrophy, 'myasthenic myopathy', 'late-life' muscular dystrophy and carcinomatous myopathy. It seems probable that these many diseases did not emerge from obscurity to afflict the human race for the first time in the twentieth century but rather that they have only lately been differentiated from other neuromuscular disorders. Their identification has been achieved by assiduous clinical study, assisted by the more frequent use of special laboratory procedures such as muscle biopsy and electromyography.

A voluminous medical literature has accumulated concerning each of these clinical entities but, unfortunately, it has done little to aid us in our understanding of them or in clarifying their relationships one to another. Moreover, the terminology has also remained a source of confusion for at some time or other nearly all of them have been designated as polymyositis, with the implication, often quite erroneous as we shall see, that they are all due to an infection or an inflammatory process. Part of the difficulty has unquestionably arisen from the fact that the number of recorded cases of some of these conditions is few; and some of the descriptions of clinical and pathological data have been so meagre and imprecise that it cannot be determined whether they all represent separate diseases or simply several variants of a few basic disorders of muscle.

It is with the object of analysing critically some of these problems against the background of a personal experience with a series of forty cases, collected from two large general hospitals in the north-eastern United States and north-east England, that we present the present monograph. Clinically all of our cases showed, at some stage of the illness, unmistakable symptoms and signs of a generalised disease of muscle with weakness and atrophy. Pathologically, all cases in which muscle sections were obtained at biopsy or autopsy

revealed a degenerative and often an inflammatory process of a type and degree which, in combination with the clinical picture, set them apart from progressive muscular dystrophy. The applicability of the term 'polymyositis' in the denomination of such a varied group of cases will be considered in Chapter 10. It should be stressed that cases of unequivocally infective (bacterial or virus) myositis were excluded and that we are considering the 'idiopathic' disease.

The text of the present communication will begin with a synopsis and critical review of published reports concerning each of the muscle disorders under consideration, in order to orientate the reader in this confusing field. This will be followed by a detailed analysis of the clinical and pathological findings in our own cases which are reported individually in the Appendix. Finally, we shall attempt to make certain deductions concerning the nature of the morbid process or processes involved and to draw certain conclusions as to their inter-relationship.

This work was begun during the tenure by one of us (J. N. W.) of a Nuffield Foundation Fellowship in the Massachusetts General Hospital and was continued during the tenure of the King's College Travelling Fellowship in Medicine in the Neurological Research Unit, the National Hospital, Queen Square. It was aided by an initial grant from the Julius Marks Research Fund of the Massachusetts General Hospital and by a research grant awarded to one of us (J. N. W.) by the Muscular Dystrophy Associations of America, Inc.

We wish to thank Drs J. B. Ayer, C. S. Kubik, W. Bauer, F. Albright, H. Viets, R. S. Schwab, C. Miller Fisher and R. McCombs of Boston; Professor F. J. Nattrass, Drs H. G. Miller and C. Strang of Newcastle upon Tyne; and Dr T. C. Studdert of Carlisle for permission to refer to patients who were under their care. We are also grateful to Drs B. Castleman and E. P. Richardson, Jr., of Boston and to Professor J. B. Duguid and Dr R. Schade of Newcastle for making available to us pathological material from many of the cases. In this connection we must thank Miss M. Carroll and Mrs N. Shaffer of Boston for technical assistance. Many of the photomicrographs were prepared in the Department of Photography of the Massachusetts General Hospital under the supervision of Mr Donald Withee; photographic reproductions of radiographs in Case 32 are published by permission of Dr Fuller Albright. Other photographic work was carried out in the Department of Photography, King's College, Newcastle upon Tyne, under the direction of Mr C. J. Duncan, and the charts were prepared by Mr A. H. Prickett in the Photographic Department of the National

Hospital, Queen Square, London. Fig. 1 is published by kind permission of Professor F. J. Nattrass and the Editor of the *Proceedings of the Royal Society of Medicine*, and the Editors of *Modern Trends in Neurology*. Miss E. F. Grzebieniowska gave valuable help in tracing patients; Mrs Ruth Simonds of Boston, Miss P. Smith of London and Miss S. M. Whillis of Newcastle upon Tyne have given invaluable help in the preparation of the manuscript.

Finally, we would like to thank Mr Charles Macmillan and the staff of E. & S. Livingstone, Ltd, for all the valuable advice they have given in the preparation of this book.

NEWCASTLE UPON TYNE
BOSTON, MASS.
1957

JOHN N. WALTON
RAYMOND D. ADAMS

CONTENTS

CHAPTER 1

POLYMYOSITIS AND RELATED CONDITIONS: A CRITICAL REVIEW OF PRESENT KNOWLEDGE

DERMATOMYOSITIS AND POLYMYOSITIS

Introduction

IT IS generally acknowledged that the first recorded case of this type was that described by Wagner (1863) who introduced the term 'polymyositis'. He reported an acute generalised muscular affection, with skin involvement, which progressed rapidly to a fatal outcome within six days. In a similar case described by Potain (1875) the illness was less acute, but the patient died from bronchopneumonia between four and five months after the onset. A further report by Wagner appeared in 1887, while, in the same year, Hepp presented a full account of the clinical features of a similar disorder under the name of pseudotrichinosis, and Jackson, a Boston physician, contributed a case report, the first from the United States, under the title 'myositis universalis acuta infectiosa'. In Hepp's case there were no skin lesions, the picture being that of a subacute polymyositis, but Unverricht (1887) stressed the almost invariable occurrence of lesions in the skin as well as in the muscles and coined the name 'dermatomyositis'. Subsequently, the same author (Unverricht, 1891) described the pattern of muscular involvement, noting the characteristic affection of trunk and proximal limb muscles, but appreciating that virtually any striated muscle in the body could be involved. He also delineated the clinical course of the disease, pointing out that not all cases were fatal; one of his patients with an acute, severe form of the disease made a complete recovery. From these and numerous other reports, particularly in the French and German literature, the clinical and pathological features of these conditions were gradually defined and were

distinguished from those of bacterial and parasitic myositis. In 1899 and in 1903 Oppenheim drew attention to the occasional involvement of mucous membranes and of ocular and cardiac muscle and pointed out that the skin lesions might be sclerodermatous in character. A chronic form of the disease was described by Petges and Cléjat in 1906 and they stressed the extreme degree of atrophy and sclerosis of the skin (poikiloderma) which could eventually develop.

Gowers (1899) and Batten (1899), who were the first to report cases from Great Britain, used the title 'polymyositis' for the disease, despite the fact that they described changes in both skin and muscle. Subsequently, most of the published accounts have reflected an uncertainty as to the relationship between dermatomyositis and other acute and chronic muscle diseases without skin lesions. The terms polymyositis and dermatomyositis were used almost indiscriminately by the early authors and it was more or less assumed that skin changes were an integral part of the disease. This view has remained current up to the present day and until the last few years there has been scanty recognition of the fact that a condition of this nature may occur without recognisable changes in the skin. A comparison of cases of dermatomyositis and polymyositis reported more recently will underline this fact. There is ample evidence that the presence or absence of skin lesions does not depend upon ætiology, nor does it appear to be related to the pattern of pathological changes in the muscle. These questions will be considered in detail in subsequent chapters.

Dermatomyositis

Steiner, in 1903, reported a case from the Johns Hopkins Hospital under the name dermatomyositis, even though skin changes were minimal; he also reviewed the twenty-eight cases which had been published up to that time. His admirable description of the clinical picture and his definition of dermatomyositis as an acute, subacute or chronic disease of unknown origin characterised by œdema, dermatitis and multiple muscle inflammation, could hardly be improved upon today, so far as the commonly accepted picture of dermatomyositis is concerned. However, in common with many authors writing subsequently, he failed to recognise that other cases occurred with identical

muscle changes but without skin lesions, pain, tenderness or constitutional symptoms. That this limited concept of the disease is retained today may readily be verified by reference to the many reviews which have been written upon this subject. Karelitz and Welt (1932) collected seventy-five cases from the literature, while Schuermann, in 1939, was able to review two hundred and sixty-three cases, of which forty-seven were in children. O'Leary and Waisman (1940) described forty personal cases and Selander (1950) reviewed twenty-two occurring in childhood, of which three were personal, while Sheard (1951) reported twenty-five cases and Wedgwood *et al.* (1953) another twenty-six, all children, and seen between 1916 and 1952. Each of these authors referred to very occasional cases in which skin lesions were absent or minimal but laid no stress on this finding and the same omission is noted in the recent review by Domzalski and Morgan (1955). Matthews and Burne (1953) pointed out that dermatomyositis could resemble polyneuritis, myasthenia gravis or bulbar palsy and that skin changes could be minimal; however, like Wilson (1954), they did not recognise that they could be absent and they went on to state that the resemblance to progressive muscular dystrophy could seldom be close. Ford (1952), too, while recognising that there may be no cutaneous involvement and that the condition might resemble a polyneuritis, failed to take account of that form of the disease which, by its chronicity and lack of skin lesions, shows many of the characters of a muscular dystrophy.

Apart from isolated reports which received little attention, only Keil (1940) remarked upon the resemblance between myositis and dystrophy, saying that some of his cases of dermatomyositis had been diagnosed as myopathies and that 'Neurologists seem hardly to be familiar with this peculiar condition in its various and manifold phases'. Recent reports (Adams *et al.*, 1953; Eaton, 1954; van Bogaert *et al.*, 1955; Garcin *et al.*, 1955; Nattrass, 1954, 1956; Walton, 1956; Coërs, 1956) have underlined the truth of this assertion and have stressed that the accepted concept of dermatomyositis is too rigidly defined. Not only are there subacute and chronic cases in which skin changes are minimal but an essentially similar condition without cutaneous manifestations is much more common than is generally realised.

Polymyositis

The existence of an acute form of polymyositis in which there may be striking œdema of the muscles and subcutaneous tissues but no recognisable lesion of the skin, has been recognised since Hepp's report in 1887. The condition runs a course very like that of acute dermatomyositis and may occur at any age, though it seems to be most common in childhood. The case of 'myatonia congenita' described by Bovet in 1936 was a probable example of this condition occurring in an infant of three weeks. Two children afflicted by this form of the disease have been reported by Radermecker and van Bogaert (1955), and similar cases are referred to by Garcin *et al.* (1955). There seems to be no reason why acute hæmorrhagic polymyositis (Marinesco *et al.*, 1934) should not be considered to be similar, as the hæmorrhages in the muscles are simply an indication of the acuteness of the disease process. It is apparent that an acute polymyositic form of polyarteritis nodosa may present with this clinical picture (Radermecker and van Bogaert, 1952) but in this condition the histological changes are characteristic of the primary arterial disease and it is clear that not all cases of acute polymyositis are of this type, despite recent assertions to the contrary (Caldwell, 1957).

The acute form of polymyositis is, however, comparatively rare and it is now apparent that the disease more commonly presents in a sub-acute or chronic form with little or no constitutional upset, pain or muscular tenderness. It is these cases which may resemble very closely muscular dystrophy, myasthenia gravis or polyneuritis of proximal distribution. They are relatively common and it is certain that many have gone unrecognised in the past. As we shall point out, no fewer than fourteen of our forty cases had been diagnosed as examples of muscular dystrophy. Furthermore, it is probable that at least six of the eight cases studied by one of us (J. N. W.) with Nattrass (1954), in which recovery had taken place from an illness previously diagnosed by eminent clinicians as progressive muscular dystrophy, were suffering from polymyositis.

The first case in which this diagnostic error occurred was probably that of Cassirer (1898); and the general failure of clinicians and pathologists to recognise the entity of polymyositis

and its mimicry of muscular dystrophy can probably be explained by the paucity of subsequent reports of cases of this type. One of the first writers to discuss the differential diagnosis of dystrophy and polymyositis was Levison, who, in 1937, described two cases with involvement of proximal muscles, one of which was fatal owing to pharyngeal paralysis and œdema of the glottis. Subsequently, Urechia and Dragomir (1943) and Furtado and Alvim (1945) each described cases showing a striking clinical resemblance to progressive muscular dystrophy. These reports received little attention. In 1950, Christensen and Levison reported six personal cases of polymyositis, four adults and two children. Two of their cases (Nos. 4 and 5) experienced muscular weakness of rapid progression, and one of these recovered completely; two others (cases 1 and 5) showed some features (muscle pain, remittent course, dysphagia, apparent response to prostigmine) which are common in dermatomyositis, but yet had no skin involvement. The remaining two cases (Cases 2 and 3) had each developed a gradually progressive weakness of proximal limb muscles; they showed pseudohypertrophy of calf muscles and seemed clinically typical of progressive muscular dystrophy; the true diagnosis was only established following muscle biopsy. Although the descriptions of muscle pathology in this report are not as detailed as one would wish and the authors tend to give rise to confusion by inappropriate use of the word 'dystrophy", it is clear that infiltrations of inflammatory cells were a prominent feature of the pathological picture in all of these cases and there seems little doubt that the patients were suffering from polymyositis.

Adams *et al.* (1953) recently reviewed the pathological changes in dermatomyositis and polymyositis and stressed the methods of distinguishing these appearances from those of progressive muscular dystrophy. We now believe that the boundaries of the clinical syndrome of polymyositis presented in this work were too narrow. For instance, although the accepted clinical manifestations of dermatomyositis were described under the heading of acute polymyositis, sufficient emphasis was not placed upon those cases in which the skin changes may be minimal and easily missed. Furthermore, chronic polymyositis was depicted as an inexorably progressive condition affecting particularly the peripheral limb muscles.

As we shall point out, we have not observed any case conforming with the latter description in the patients of the present series. The disease practically always began in the proximal limb muscles in our cases, although the distal muscles were sometimes affected simultaneously. Our recent experience has also led us to modify and extend certain of the pathological observations described by one of us (R. D. A.) in this work.

That the syndrome is gradually receiving more widespread recognition is evident from recent reviews. Zierler and Lilienthal (1953) described two cases, one of which could not be distinguished clinically from progressive muscular dystrophy save for the rapidity of progression of the disease. Eaton (1954) has also discussed the subject in considerable detail, and has underlined the usual absence of pain and constitutional upset and the frequency with which this condition has been called muscular dystrophy. He reported a series of forty-one cases, of which seventeen showed no cutaneous manifestations. In some of the remaining twenty-four the cutaneous manifestations were primary, in others they did not appear until muscular weakness had been present for a considerable time, while in eight cases they were minimal and could easily have been overlooked. The author suggested that these cases should continue to be called dermatomyositis, while the term polymyositis should be reserved for the remainder. In patients who had one of the other 'collagen' diseases along with muscle involvement he suggested that the diagnosis should be qualified as, say, 'polymyositis with rheumatoid arthritis'. The importance of electromyography and muscle biopsy in diagnosis was indicated, but it was also pointed out that sometimes the histological changes in the muscle were minimal, seeming insufficient to explain the comparative severity of the patient's symptoms. Despite this difficulty, the author felt that polymyositis gave a clinical picture sufficiently distinctive to be regarded as a definite clinical entity.

Additional support for this view has come from the reports of van Bogaert and Radermecker (1954), van Bogaert *et al.* (1955), Garcin *et al.* (1955), Richardson (1956) and Coërs (1956). Van Bogaert *et al.* have described in detail seven cases of chronic polymyositis in which the clinical picture was that of a myopathy of late onset, while Garcin *et al.*, in an exhaustive review,

consider the clinical and pathological features of the syndrome in considerable detail. Richardson points out that of fifty-two cases of myopathy referred to him for electromyography, thirteen proved to be examples of polymyositis, while Coërs, in paying tribute to the pleomorphic clinical presentation of the syndrome, also describes a pseudomyopathic form.

It would not be appropriate at this point to consider the ætiology, pathology, prognosis and treatment of polymyositis, as these aspects of the disorder will receive full consideration in subsequent chapters. However, there is general agreement that in many, if not most cases of this syndrome, the disease process is related to others in the 'collagen' (Klemperer *et al.*, 1942) or 'connective tissue' (Klinge, 1929) group. Furthermore, it is apparent that some cases may recover spontaneously while others may respond to adrenal steroid or ACTH therapy.

Conclusions

It may, therefore, be concluded from published work that although the classical clinical picture of dermatomyositis and of acute polymyositis has been recognised for many years, only recently has it been realised that polymyositis can occur in both subacute and chronic forms, without skin involvement, and frequently lacking constitutional symptoms, muscle pain and tenderness. In many such cases it may be difficult or impossible to distinguish the condition clinically from progressive muscular dystrophy; and such a distinction is not of purely academic interest as some cases of polymyositis may recover spontaneously, and others may respond to treatment.

NEUROMYOSITIS

Senator (1893) was the first to report a case of dermatomyositis in which there was sensory loss of peripheral distribution and he suggested that this finding indicated involvement of peripheral nerves as well as muscle. However, it is important to note that sensory impairment was present in only one of his cases, although the peripheral nerves were tender in others; and it is impossible to be certain from his descriptions that his patients were suffering from dermatomyositis. Adams *et al.* (1953) have suggested that in some cases sensory loss may be due