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The next issue will treat of: **PARKINSONISM**

Editorial

Tenemos el gratisimo placer de anunciar a nuestros lectores la incorporación al Comité Consultivo, de una figura consular de la Medicina contemporánea el Prof. Dr. Derek Denny-Brown, vastamente conocido por sus importantes contribuciones en el campo de la Neurologia clínica y experimental.

Le damos en este número nuestra más cordial bienvenida y estamos particularmente orgullosos y honrados de contarle entre los valiosos consultantes que nos asesoran con su reconocida versación y experiencia para que cada número publicado sea de real utilidad e interés para los lectores de la Revista Internacional de Neurologia.

El estudio de las afecciones musculares ha sido siempre motivo de preocupación para los médicos y particularmente los neurólogos puesto que es a éstos a quienes se recurre generalmente cuando se está frente a una deficiencia motora.

En los últimos años el interés se ha multiplicado al punto que actualmente es uno de los capítulos en que más se investiga y se publica.

Pero si bien son los neurólogos los que más se preocupan por organizar y realizar las pesquisas, el tema desborda hoy los lindes de la neurologia y está totalmente ensamblado a varios capítulos pertenecientes al amplio campo de la medicina interna.

Han determinado la actual situación varios factores; el progreso de la electromiografía que se ha constituido prácticamente en una especialidad y que tiene cada día más cultores; la práctica casi rutinaria de la biopsias musculares, hoy realizada en forma selectiva con el auxilio del registro eléctrico y con estudios histológicos especiales; la creciente importancia de la bioquímica y los nuevos conceptos acerca del metabolismo muscular; las relaciones de ciertos sufrimientos musculares con las enfermedades del colágeno.

El músculo como otras partes del organismo tiene su propia manera de reaccionar que en cierto modo se repite frente a distintos agentes agresivos.

En una miositis se observa junto al daño más o menos aparente del parénquima y elementos intersticiales del músculo, exudación de plasma, e infiltración por neutrófilos u otras células de tipo inflamatorio.

El reconocimiento de la presencia de un factor bacteriano, parasitario o virósico da la prueba del origen infeccioso de la enfermedad. Cuando falta esta evidencia entonces puede plantearse la duda con respecto al origen de la lesión.

En la polimiositis no están presentes los agentes patógenos mencionados;

pero la naturaleza del cuadro anatómico microscópico corresponde a las lesiones inflamatorias.

En estos casos la reacción inflamatoria del músculo suele presentarse combinada con reacciones similares de piel y nervios; entonces se configura la dermatomiositis (piel y músculo), la neuromiositis (nervio y músculo).

Así queda integrando el grupo de las colagenosis. ¿Cuál es la causa de esta enfermedad? ¿Infección por virus? ¿Un trastorno nutricional? Su característica histopatológica es semejante a la de la carencia experimental de vitamina E. ¿Reacción del organismo en su sector muscular a distintas causas? Con lo cual se sugiere que podría tener distintos orígenes. Difícil es dar una respuesta satisfactoria.

Las primeras observaciones sobre esta enfermedad fueron hechas hace ya casi un siglo por Wagner (1863) quien acuñó el término de poliomyositis. Después se sucedieron distintas publicaciones y en el siglo pasado cabe mencionar los nombres de Potain, Unverricht, Happ, Jackson, Strumpell, Oppenheim, autores que se han ocupado del tema. En 1903 Steiner dio de la Dermatomiositis una definición clínica que hasta ahora conserva su validez: "enfermedad aguda, subaguda o crónica de origen desconocido caracterizada por comienzo gradual, con prodromos vagos e indefinidos, seguidos por edema, dermatitis y múltiple inflamación de los músculos".

Importa señalar que manifestaciones de miositis pueden observarse integrando otras enfermedades del colágeno como el lupus eritematoso sistémico, la periarteritis nodosa, la escleroderma y la artritis reumatoidea.

La Revista Internacional de Neurología tiene el honor de ofrecer este tema realizado por notabilidades como el Prof. Dr. Raymond Garcin y el Dr. Jean Lapresle de París, el Prof. Dr. Gilbert Glaser de New Haven; los Dres. C. Serra y Lucio Covello de Palermo y los Dres. David B. Barwick y John N. Walton de Newcastle upon Tyne.

Estimamos que los lectores recibirán con beneplácito este número dedicado a la Polimiositis.

VICTOR SORIANO

Editorial

We have great pleasure in announcing to our readers that henceforth Dr. Derek Denny-Brown one of the world's most prominent neurologists will be a member of our Advisory Board.

Dr. Denny-Brown is widely known for his important contributions in the clinical and experimental neurology. In this number we give him a very cordial welcome and we are particularly proud and honoured to have him among our invaluable consultants that advise us with their recognized experience and knowledge.

The study of muscular ailments has always been a source of preoccupation for doctors especially those dedicated to neurology, because they are generally consulted when motor deficiencies occur.

In recent years the interest in these diseases has augmented considerably so much that at present they are one of the phases of medicine to which more publications and investigations are devoted.

But even though nowadays the neurologists are the people more concerned in organizing and carrying on investigations in this subject, we find it also totally connected to different aspects within the ample field of Internal Medicine.

Various factors have determined the current situation: the progress of electromyography which has reached the point of practically a specialty which everyday attracts more practitioners; the almost routinary performance of muscular biopsies, actually done in a selective manner with the aid of the electrical recording and with special histopathological studies; the growing importances of Biochemistry and the new concepts about muscular metabolism, and the relation that certain muscular ailments have with the collagen diseases.

The muscle, like any other part of the organism has its own form of reaction that in a peculiar manner repeats itself when facing certain aggressive agents.

In a myositis this reaction is observed along with the more or less noticeable injury of the parenchyma and the interstitial elements of the muscle, plasma exudation, and infiltration by neutrophils or another cell of inflammatory type.

The evidence of the presence of a bacterian, parasitic factor or of virus confirms the infectious nature of the illness.

When there is lack of evidence regarding its infectious character, the origin of the lesion is doubtful.

In polymyositis the etiologic agents above mentioned are not present, but its anatomic microscopical picture corresponds to those due to inflammatory lesions.

In these cases the muscle inflammatory reaction may be seen combined with similar skin and nerve reactions, thus constituting the dermatomyositis (skin and muscle), the neuromyositis (nerve and muscle).

Thus they form part of the collagen diseases group. What is the origin of this illness? Is it virus infection? Is it due to nutritional disturbances? Since its histopathologic characteristic is similar to those seen in cases of vitamin E deficiency. Is it a reaction in the muscular regions due to sundry factors? This suggests that it can have more than one origin. It is difficult to find a satisfactory answer.

Nearly a century has passed since the first observations on this illness. To Wagner (1863) corresponds the credit for giving the name of Polymyositis to this kind of ailment. Afterward it is worthwhile to mention the names of Potain, Unverricht, Happ, Jackson, Strumpell, Oppenheim, authorities who during the last century devoted studies to this subject. In 1903 Steiner gave to the Dermatomyositis, a clinical definition that has remained valid up to now to designate "an acute, subacute or chronic illness of an unknown origin, characterized by a gradual onset with vague and undetermined prodrome, followed by edema, dermatitis and multiple muscles inflammatory reaction".

In many instances myositis appears as a part of the picture of other collagen diseases such as acute systemic lupus erythematosus, periarteritis nodosa, scleroderma and rheumatoid arthritis.

The International Journal of Neurology has the honour of offering this intriguing neurological topic to its readers realized by outstanding specialists: such as Prof. Raymond Garcin and Dr. Jean Lapresle from Paris, Prof. Dr. Gilbert Glasser, from New Haven, Drs. Carlo Serra and Lucio Covello from Palermo and Drs. David B. Barwick and John N. Walton from Newcastle upon Tyne.

It is our hope that this issue will be very wellcome by the numerous specialists interested in the latest news about Polymyositis.

VICTOR SORIANO

Polymyositis in the Collagen Diseases

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Aided by a grant from the Muscular Dystrophy Associations of America.

The original report, in 1863, of the condition known as polymyositis(19) was of an acute generalized muscular disorder with skin involvement which progressed rapidly to death in several days. During the next 40 years there were a number of similar descriptions generally associating both skin and muscle manifestations(9). By 1903 the disorder of dermatomyositis was presented in detail(18) as an acute, subacute or chronic disease of unknown origin characterized by edema, dermatitis and muscle inflammation. Only in more recent years has the concept of polymyositis been broadened(3, 6, 20). It is now realized that the disorder of muscle may exist alone, without any other systemic involvement, and must be differentiated from other forms of primary myopathy. However, many instances of polymyositis are associated with the presence of a more generalized collagen disease in the patient. This is not only myositis appearing with cutaneous lesions as in dermatomyositis, but also as part of the picture of other collagen diseases such as acute systemic lupus erythematosus, periarthritis nodosa, scleroderma and rheumatoid arthritis. Myositis existing alone may represent a localized disorder of collagen. These collagen diseases are grouped according to a morphologic concept as disorders of diffuse involvement of connective tissue. Whether they are intimately related with regard to causative factors and represent a single entity is still not clear. Clinical syndromes in many instances are not definitively delineated, and many cases occur which do not fit into any one specific diagnostic category. The general clinical characteristics of acute systemic lupus, periar-

teritis nodosa, scleroderma and dermatomyositis are presented in Table I, which indicates differences and similarities(7).

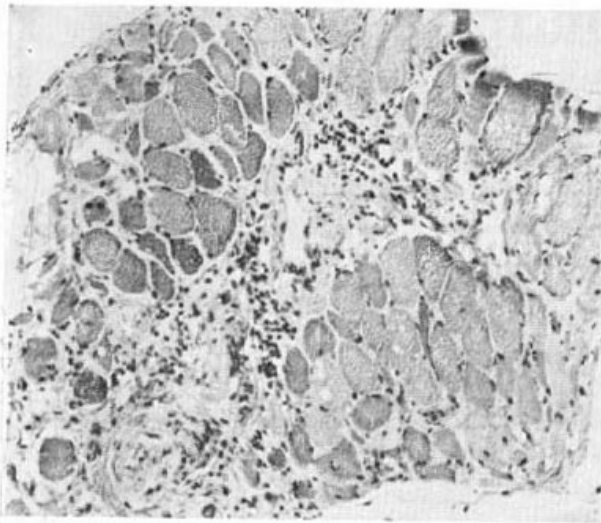
The intensity of the clinical manifestations in the collagen disease may be quite variable. In some instances the signs and symptoms in the muscles are predominant and those of the general collagen disease such as in the skin, joints, heart and kidneys are mild and unobtrusive. In other cases, however, the symptoms of the collagen disease are the most predominant and the muscular involvement appears in less intense fashion.

Dermatomyositis

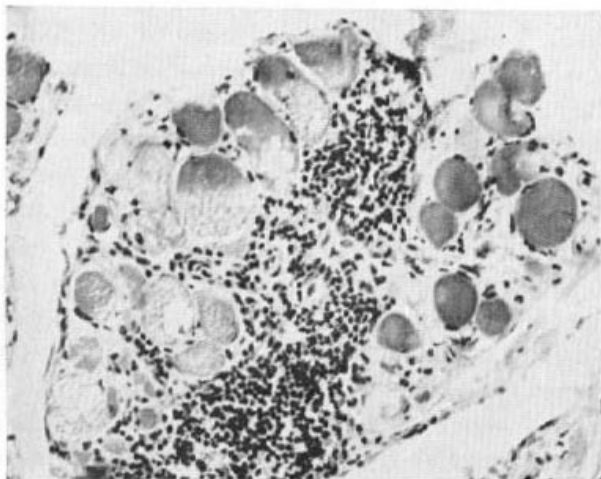
This acute, subacute and chronic collagen disorder affects primarily the skin and skeletal muscles (1, 18, 20). It has a widespread incidence from infancy to old age, and is more common in females. A significant number of cases have been associated with carcinoma elsewhere in the body, especially pulmonary and gastrointestinal. The basic etiology, however, is not known.

The arterioles in the skin, subcutaneous tissue and muscle have hyperplastic walls with infiltrations. In some cases, however, vascular lesions are minimal. Cutaneous edema, atrophy and infiltrations develop. The skeletal muscles (Figure 1) contain both degenerative and regenerative changes with necrosis, fragmentation and atrophy of fibers, vacuolization, great variation in fiber size, proliferation of sarcolemma nuclei and eventual fibrosis with increase in endomysial collagen. Interstitial infiltrations may be marked and consist of lym-

Figure 1. — MYOSITIS IN DERMATO-MYOSITIS. HEMATOXYLIN AND EOSIN STAIN



a. — Interstitial infiltrations, fiber degeneration and necrosis around vascular lesions. X 240



b. — Swelling and vacuolar degeneration of muscle fibers. Some fibers necrotic and atrophic. Heavy lymphocytic infiltration. X 300

phocytes, monocytes, plasma cells, and rarely leucocytes, usually perivascular, but not always. Infrequently, perineural infiltrations are present. The terminal nerve fibers may have complex arborizations, and the motor end plates, degenerative changes(2). Muscle biopsy is useful in establishing categorical diagnosis, but patchy muscular involvement may be misleading, and the findings in certain stages are non-specific.

The clinical onset is usually insidious but may be acute, with fever, patchy, cutaneous erythema and edema, myalgia, weakness, arthralgia and vasomotor disturbances. The skin manifestations when present are diverse, and characteristically appear first in the face, especially about the nose and cheeks, often with a light purple, "heliotrope", hue. The upper extremities then become involved, especially the extensor surfaces of the hands and nail beds. Telangiectases are common. Raynaud's phenomena are frequent and ulcerations may occur. The skeletal muscle disorder may precede or follow the presence of skin lesions. The latter may remain quite inconspicuous. Typically, proximal symmetric weakness appears, involving the shoulder and pelvic girdles with or without muscle tenderness. Muscle pain is less common in the more chronic cases. Eventually, facial, jaw, pharyngeal, tongue and distal skeletal muscles become involved. Symptoms similar to myasthenia gravis may appear in this, and other collagen diseases. Dysphagia is present in over one-half the cases. Pharyngitis and stomatitis may occur. Ophthalmoplegia is rare. In severe instances respiratory paralysis ensues. Atrophy is variable and visible fasciculations are unusual. The deep reflexes, normal at first, eventually become inactive. Contractures may develop in chronic instances and the muscles become indurated.



c. — Necrosis of muscle fibers. Proliferation of sarcolemmal nuclei. Intramuscular fibers with increased collagen. Basophilic fibers with centrally placed nuclei and prominent nucleoli. Possible regeneration. X 300

The electromyogram often shows increased irritability, fibrillation potentials, increased numbers of low amplitude polyphasic discharges and occasional myotonic-like activity. Distal sensory deficit has been reported as a rare occurrence, probably then related to an associated neuropathy. In some instances the muscular disorder produces myoglobinuria and more frequently, creatinuria. Remarkably high levels of serum transaminase may be present. Blood alterations otherwise include leukocytosis or leukopenia, anemia, rarely eosinophilia, elevation in erythrocyte sedimentation rate and hyperglobulinemia. Signs of general disease may be hepatosplenomegaly, lymphadenopathy, joint swellings and severe weight loss. Clinical evidence of cardiac muscle disorder or pericarditis is uncommon, although electrocardiographic abnormalities are relatively frequent. Renal involvement may occur producing albuminuria and, infrequently, uremia. Although an elevated basal metabolic rate is common, there is no evidence of thyroid dysfunction. Generalized osteoporosis, subcutaneous calcinosis and skeletal deformities develop in advanced cases. Calcium deposits may appear as long as three to five years after the onset of the disease and may appear in subcutaneous tissue, tendons and in the muscle itself(12). These disseminated calcifications may be particularly extensive in children.

The course is extremely variable with remissions and exacerbations, a more chronic and insidious development being more common in adults, as a "later life myopathy". The clinical picture then is similar to a limb-girdle muscular dystrophy. Fifty to sixty percent of patients die within two years and the remainder experience spontaneous remissions or residuals in a chronic course with permanent atrophy, weakness, contractures. The prognosis is more grave in the older age group.

Scleroderma

Scleroderma, or progressive systemic sclerosis, is characterized by focal or generalized thickening and induration of the skin and other tissues, especially certain viscera(11). Muscular atrophy may be promi-

nent. The disease usually occurs between the ages of 30 and 50, and is more common in females. In many instances there appear to be transitional phases between dermatomyositis, scleroderma and systemic lupus. The etiology is obscure but it has been related to endocrine dysfunction, neurotrophic factors, hypersensitivity and infections, with no definite conclusions.

The pathology of scleroderma is that of swelling, proliferation and fusion of collagen fibers, as well as fibrinoid degeneration and infiltrations in small arteries and arterioles in the skin, skeletal muscles, heart, lungs, gastrointestinal tract and kidneys. Atrophic changes also develop in the skin and mucous membranes. The muscular lesions (Figure 2) are those of fiber degener-

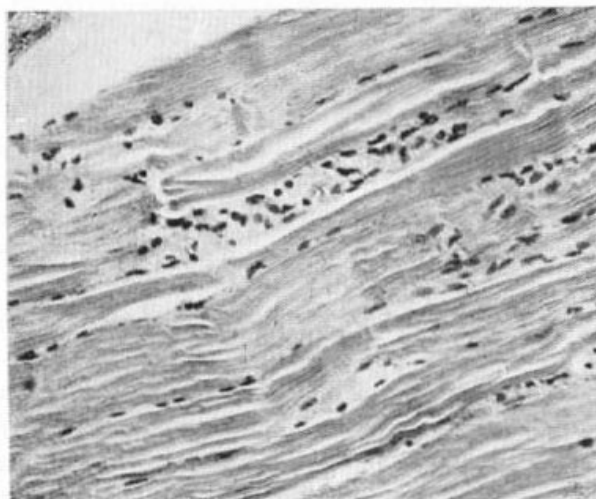


Figure 2. — *Myositis in scleroderma. Muscle fiber degeneration with infiltration. Hematoxylin and eosin stain. X 300*

ation and atrophy, and cellular infiltrations, both diffuse and interstitial. The latter may produce nodular masses.

The clinical onset is usually insidious with fever, focal and diffuse edema in the skin and peripheral vasomotor disturbances particularly of the Raynaud type. Eventually, the characteristic skin changes occur, especially in the face, neck and upper extremities, with a taut thickening and shiny waxy appearance, associated frequently with pigmentary variation, cyanosis, erythema and loss of hair. Limitation of motion and contractures are frequent. Symptoms of muscle involvement may appear early in the disease(15). Facial mobility is

lost. Trophic ulcerations are common, especially in the fingers. The involved muscles are tender, indurated and atrophic. Distal muscle disorder may be prominent. Hoarseness and dysphagia are common. A mild peripheral neuropathy may occur, producing paresthesias and sensory deficits. Systemic symptoms related to joint, gastrointestinal tract and cardio-pulmonary involvement. The prognosis generally is poor, at least one-half of the patients are dead within five years, and the surviving 50 percent usually have a prolonged course with debilitation and recurrent infections.

Systemic Lupus Erythematosus

Systemic or disseminated lupus erythematosus is usually a prolonged generalized disease involving collagen tissues throughout the body, with acute exacerbations and remissions, occurring mainly in females (85 % of cases) and most commonly between the ages of 15 and 40 (5,7,10). The etiology is unknown, however, a number of cases have been precipitated by exposure to sunlight and general infections.

The lesions are primarily vascular with fibrinoid degeneration of collagen in the walls of small arteries and arterioles, eventually producing conglomerate masses of fibrinoid tissue, destruction of muscularis, intimal and elastic tissue elements and occlusion. Endothelial proliferation may contribute toward thrombus formation. Synovial and serous membrane lesions are frequent. The muscular lesions (Figure 3) are interstitial myositis and acute hyaline necrosis as well as the vascular degenerations. Rarely, extensive vacuolization of muscle fibers occurs with hypertrophy and hyperplasia of sarcolemmal nuclei (14).

The major general symptoms and signs of acute lupus are those of febrile illness and polyarthritides, characteristic butterfly cutaneous lesion of the face, pleural-pulmonary, pericardial-cardiac and renal involvement. Splenomegaly is frequent. Symptoms of polymyositis may be striking, the inflammatory infiltrations and degenerations in the muscles producing weakness and tenderness in distribution similar to dermatomyositis. Neurologic lesions may occur in

the brain, the spinal cord and peripheral nerves with varied symptoms depending on location of the lesions.

A number of instances have been described of transitional clinical pictures with features of acute disseminated lupus and dermatomyositis. This type of occurrence has given rise to the suggestion that dermatomyositis, scleroderma and acute lupus be considered as various forms of the same underlying disease, "viscero-cutaneous-collagenosis" (13).

The associated hematologic disturbances in acute lupus often are significant with anemia, thrombocytopenia and leukopenia. There may be hyperglobulinemia and anti-complementary or false positive serological tests for syphilis. The bone marrow and

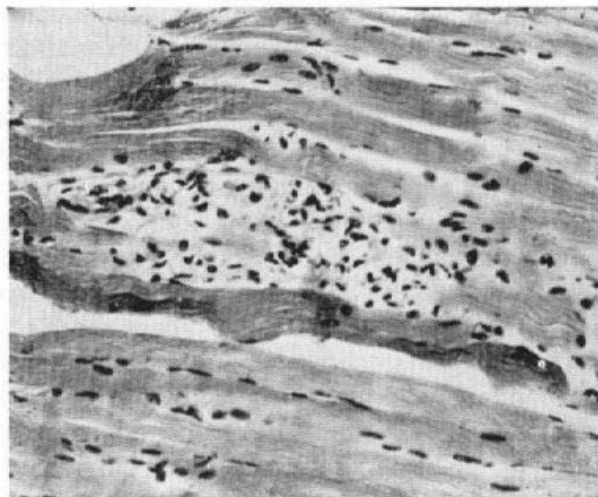


Figure 3. — Myositis in acute lupus erythematosus. Necrotic degeneration of muscle fibers with infiltrations. Hematoxylin and eosin stain. X 400

blood usually contain characteristic lupus erythematosus (LE) cells. This finding and the more recently determined lupus globulin nucleoprotein reaction (4) have led to increasing diagnosis of this disorder and a more detailed analysis of its natural history.

The course and prognosis in lupus are very variable. At least 20 percent of the patients survive more than five years, 78 percent surviving at least one year. Spontaneous remission occurs in 40 percent and is repeated in another 20 percent of cases. Renal failure and severe infections are frequent causes of death.

Periarteritis Nodosa

This is a subacute or chronic systemic disease due to a necrotizing arteritis within joints, muscles, viscera and nervous system, at least four times more common in males, and with an age incidence from infancy to late adult life, but especially between the ages of 20 and 40 (16, 17). Etiology is unknown, however, a hypersensitization reaction may be involved, since in some patients the disease apparently has been produced by sensitization to heterologous serum or to drugs such as sulfonamides and penicillin. Experimentally, lesions of necrotizing arteritis may be produced in animals sensitized by foreign proteins. In most clinical instances, however, evidence of sensitization is not present.

The basic lesion is an inflammatory reaction in the walls of the small arteries and arterioles, a panarteritis, with infiltration by polymorphonuclear leukocytes, lymphocytes and eosinophils. Necrosis of muscle and elastic fibers cause the formation of multiple small aneurysms with rupture and hemorrhage, and later fibrosis. Proliferation of intima often leads to thrombosis and infarction of supplied tissue. The fibrotic process produces nodules along the arteriole wall. Lymphocytosis and interstitial myositis may occur. There may be slight involvement of veins. The vascular lesions of periarteritis commonly involve the vasa nervorum of peripheral nerves, causing neuropathy. Lesions are common in the muscles in periarteritis nodosa (Figure 4), and muscle biopsy is a productive diagnostic procedure. The hemorrhagic and infarctive lesions differ from those of the other forms of polymyositis.

This disorder has extremely varied symptomatology. The onset may be abrupt or insidious. Early general manifestations are fever, weight loss, dyspnea, cough, malaise, headache, tachycardia, generalized weakness, and pains in joints, muscles and the abdomen. Further progression may involve any region of the body such as the skin with purpura, nodular and erythematous lesions, kidneys with hematuria and uremia, cardiovascular with hypertension and pericarditis, pulmonary with asthma, he-

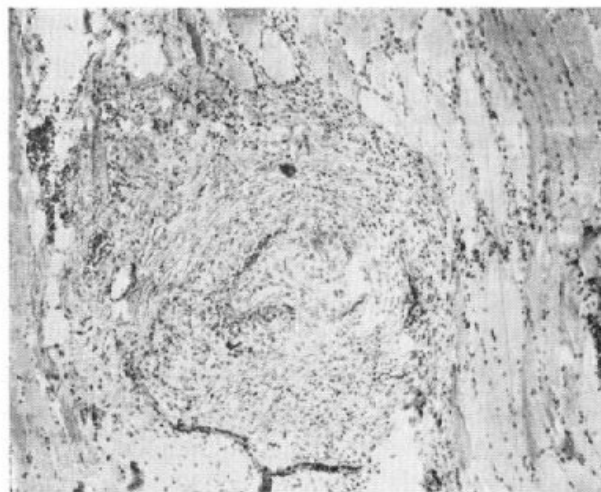


Figure 4 a.

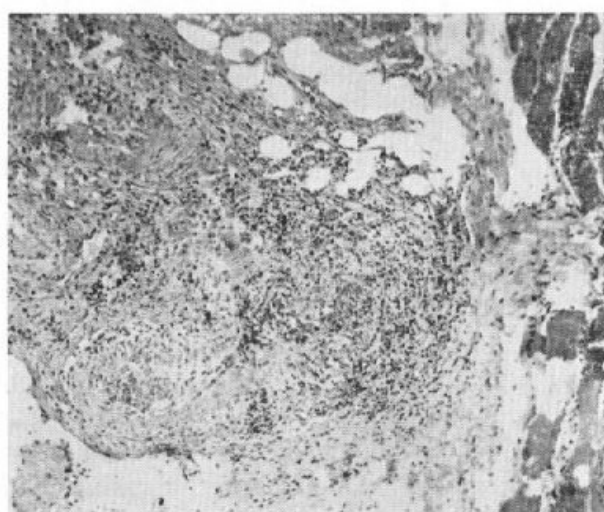


Figure 4 a. and b. — "Myositis" in periarteritis nodosa. Periarteritic nodules with proliferative vascular lesions. Granulomas in infarcted muscle, with phagocytosis, infiltrations and fibrosis. Hematoxylin eosin stain. X 125

moptysis and pleurisy, and gastrointestinal with nausea, vomiting and diarrhea. Anemia, leukocytosis or leukopenia, eosinophilia and hyperglobulinemia also occur. Focal or disseminated central and peripheral nervous system symptoms appear at onset and frequently during the course of the disease. Even though the lesions of periarteritis nodosa are common in the muscles, the clinical picture is not similar to that of the polymyositis which appears in the other collagen diseases. In periarteritis nodosa a symmetric involvement of proximal musculature does not usually occur with a "pseudo-

myopathic syndrome". More often, disseminated muscle pain and tenderness are present, relatively localized, and usually the result of the muscle infarction associated with the characteristic periarteritic vascular lesions. Frequently, small lesions are present in nonsymptomatic skeletal muscles. It has been emphasized that there are no transitional states between dermatomyositis and periarteritis nodosa.

At least 50 percent of patients with periarteritis nodosa have a remission occasionally up to several years duration. The remissions usually appear, if at all, in the first two years. A duration of two years or more indicates a better prognosis. Prognosis is more grave when renal and central nervous system lesions exist.

Rheumatoid Arthritis

Rheumatoid arthritis has been included in the group of the collagen diseases. It may exist as a separate entity, or in close association with other collagen diseases, particularly systemic lupus erythematosus. In rheumatoid arthritis, a systemic disorder develops, of unknown etiology, in which symptoms of inflammatory origin appear in the joints and related structures. The course tends to be extremely variable and chronic with remissions and exacerbations. It occurs more commonly in women and may appear in infancy and later life, but particularly between the ages of 30 and 40.

The inflammatory changes occur particularly in joints, with edema, proliferation of capillaries and infiltration, producing granulation tissue and fibrosis. Subcutaneous nodules occur consisting of granulation tissue and inflammatory cells, as well as necrotic fibrinoid material. Atrophy and degeneration of muscle fibers are prominent with focal nodular infiltrates (Figure 5), mainly of lymphocytes, particularly in the endomysial and perimysial connective tissues (20). This nodular interstitial polymyositis also occurs in rheumatic fever. Disuse atrophy of muscle is common in rheumatoid arthritis.

Characteristic muscular symptoms and signs of polymyositis may develop in patients with rheumatoid arthritis. However,

at times it might be difficult to determine whether the marked muscular wasting present in patients with rheumatoid arthritis is due to actual polymyositis or disuse muscular atrophy. Often, histological lesions of interstitial myositis in this disorder may produce no symptoms or signs referable to the muscles. However, muscle biopsy might indicate the presence of infiltrations and fiber degeneration which may correlate with the clinical picture of muscular wasting. Symptoms of aching tenderness and stiffness in the muscles often appear early in rheumatoid arthritis and may be prominent throughout the course of the disease.

Commentary on Therapy of Polymyositis in the Collagen Diseases:

Specific curative therapy is not available, particularly since definite etiology is not known. General supportive measures such as bed rest, limitation of activity and use of analgesics, especially salicylates, for muscle pain, are effective in acute periods. Significant suppression of activity of the collagen disease process may be accomplished by the administrations of adrenal cortical steroids and corticotropin (7, 8). High dosages of the hormones, necessary at first, should be decreased gradually. In most instances, maintenance treatment in continuous or intermittent fashion is required.

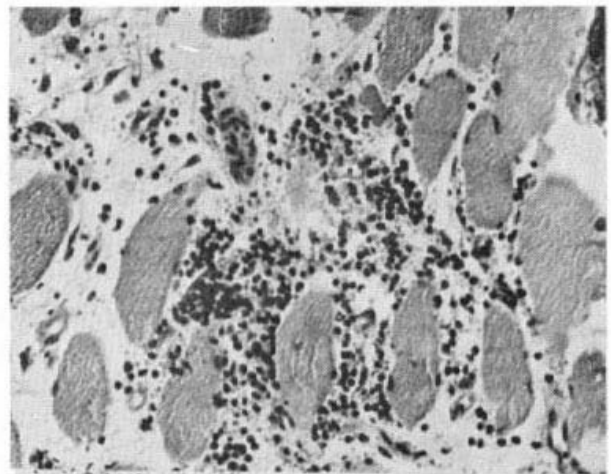


Figure 5. — Myositis in rheumatoid arthritis. Interstitial infiltrations, in nodular fashion, with lymphocytes. Some muscle fiber atrophy. Hematoxylin and eosin stain. X 350

Table I.

Comparative Clinical Features of Certain Collagen Diseases

Manifestations	Systemic Lupus Erythematosus	Periarteritis Nodosa	Dermatomyositis	Scleroderma
Sex Incidence: M: F.	1:4	4:1	1:2	1:2
Age of Onset (years)	15-40	20-40	10-50	30-50
Fever	***	***	***	**
Weight Loss	****	***	***	**
Light Sensitivity	***	—	*	*
Arthritic	***	**	*	***
Cutaneous	***	***	****	****
Central Nervous	***	**	*	*
Peripheral Nerve	*	***	*	*
Muscular	**	**	****	*
Raynaud's	**	**	**	***
Renal	**	***	—	—
Cardiac	***	***	*	*
Hypertensive	*	***	—	—
Pulmonary	**	**	—	*
Abdominal	**	****	—	—
Lymph Node	***	*	*	*
Retinal	*	*	*	*
Anemia	****	***	*	*
Leucocytes	Reduced	Increased	Normal	Normal
Eosinophilia	*	**	*	*
Urine Abnormal	***	**	*	*
LE Cells	****	—	—	—
Lupus Globulin Test	****	—	*	—

**** = 75 - 100 %
 *** = 50 - 75 %
 ** = 25 - 50 %
 * = less than 25 %
 — = chance occurrence

Close supervision is necessary to minimize the secondary effects of hypercortisonism (7,8). The fluorinated corticosteroids, especially Triamcinolone, should be avoided in the treatment of polymyositis since they may themselves induce severe weakness and an atrophic, degenerative myopathy (21). In milder degree this also has been produced by 17-hydroxycorticosteroids.

The clinical response to hormone therapy is variable, some cases being relieved re-

markably, others relatively poorly. However, a trial of hormone therapy should be given to all patients. In periarteritis nodosa, healing of vascular lesions may occur during therapy, but with increased intimal proliferation resulting in further obliteration of small blood vessels, progressive ischemia and more tissue infarction, despite satisfactory general responses.

Other medications used in acute lupus

erythematosus have been quinacrine and para-aminobenzoic acid. These may be useful in alternation with adrenal steroid administration. Temporary benefit has followed cervico-dorsal sympathectomy in some

cases of scleroderma, but regression of lesions does not occur. In all instances of severe chronic polymyositis, physical therapy may become necessary to prevent contractures and maintain muscle function.

CONCLUSIONS AND SUMMARY

Polymyositis, therefore, may precede, coexist with or follow evidence of collagen diseases including dermatomyositis, scleroderma, acute disseminated lupus erythematosus, periarteritis nodosa, and rheumatoid arthritis. The clinical picture of the polymyositis is variable but a proximal "pseudomyopathic" distribution often occurs in all these conditions with the exception of periarteritis nodosa wherein a more localized muscular involvement secondary to infarction is prominent. The muscle disorder may be the striking feature of the clinical picture in an individual case. However, it may be relatively mild when generalized signs and symptoms of the particular collagen disease are most intense. It may be suggested that all these conditions are variants of a single basic disorder of connective tissue which has many different modes of presentation. At one end of the scale there is polymyositis without constitutional symptoms, pain or skin lesions, and at the other

end, acute dermatomyositis with severe constitutional symptoms, and minimal or marked polymyositis with advanced collagen disease such as lupus erythematosus or scleroderma. However, there are probably other cases of polymyositis due to toxic and metabolic factors unrelated directly to the collagen group. The development of polymyositis in association with malignant disease may be within this category.

In most instances, the characteristic histopathological picture is most helpful in diagnosis, since features of necrosis of muscle fibers, infiltration and perivascular changes, as well as signs of muscle regeneration are prominent. The electromyographic signs are less constant. The response of many of these cases to treatment with corticotropin and adrenal corticosteroids makes the differentiation of these conditions from primary myopathy, such as muscular dystrophy, of mandatory importance.

RESUMEN

La polimiositis puede preceder, coexistir o seguir los casos de dermatomiositis, esclerodermia, lupus eritematoso disseminado agudo, periarteritis nudosa y artritis reumatoidea.

El cuadro clínico de la polimiositis es variable; pero en todos estos casos ocurre a menudo una distribución proximal pseudo-miopática excepto en la periarteritis nudosa donde predominan las lesiones musculares más localizadas, secundarias a infartos. En ciertos casos el desorden muscular puede ser la nota dominante del cuadro clínico.

Sin embargo puede existir en un plano más bien secundario cuando los signos y los

síntomas generales de la enfermedad del colágeno son muy internos. Se puede pensar que todos estos trastornos son variantes de un único desorden fundamental del tejido conectivo el cual tiene muchos modos de presentarse. En un extremo de la escala se presenta la polimiositis sin síntomas constitucionales dolores o lesiones cutáneas y en el otro extremo dermatomiositis agudas con síntomas constitucionales severos y polimiositis mínima o marcada con enfermedades del colágeno avanzadas tales como el lupus eritematoso o esclerodermia. Sin embargo hay probablemente otros casos de

polimiositis debidos a factores tóxicos y metabólicos no relacionados directamente al grupo del colágeno. El desarrollo de la polimiositis asociada con enfermedades malignas puede estar en esta categoría.

En la mayoría de los casos el cuadro histopatológico característico es muy útil para el diagnóstico, desde que son evidentes ca-

sos de necrosis de las fibras musculares, infiltraciones y cambios perivasculares lo mismo que signos de regeneración muscular. Los signos electromiográficos son menos constantes. Es de primordial importancia para diferenciar estos casos de las miopatías primarias la respuesta al tratamiento con la corticotrofina y corticosteroides.

RESUME

La polymyosite peut précéder, coexister ou suivre le cas des dermatomyosite, scléroderme, lupus érythémateux disséminé aigu, périartérite noueuse et arthrite rhumatoïde.

Le tableau clinique de la polymyosite est variable; mais dans tous ces cas il arrive souvent une distribution proximale pseudomyopatique excepté dans la périartérite noueuse où prédominent des lésions musculaires plus localisées, secondaires à infarctus. Dans certains cas le désordre musculaire peut être la note dominante du tableau clinique.

Cependant il peut exister dans un plan plutôt secondaire quand les signes et les symptômes généraux de la maladie du collagène sont très intenses. On peut penser que tous ces troubles sont des variations d'un unique désordre fondamental du tissu connectif lequel a beaucoup de manières de se présenter. Dans une extrémité de l'échelle se présente la polymyosite sans symptômes constitutionnels, douleurs ou lésions cutanées et dans l'autre extrémité dermatomyosites

aigue avec des symptômes constitutionnels sévères et polymyosite minime ou marquée avec des maladies du collagène avancées telles comme lupus érythémateux ou scléroderme. Cependant il y a probablement d'autres cas de polymyosite dus à des facteurs toxiques et métaboliques pas relationnés directement au groupe du collagène.

Le développement de la polymyosite associée avec des maladies malignes peut être dans cette catégorie.

Dans la plupart des cas le tableau histopathologique caractéristique est très utile pour le diagnostic, dès que sont évidents des cas de nécrosis des fibres musculaires, infiltrations et changement périvasculaires de même que des signes de régénération musculaire. Les signes électromyographiques sont moins constants. C'est de primordial importance pour différencier ces cas des myopathies primaires, la réponse au traitement avec de la corticotropine et corticostéroïdes.

ZUSAMMENFASSUNG

Deshalb kann die Polymyositis den Erscheinungen der Kollagenkrankheiten einschliesslich der Dermatomyositis, dem Skleroderma, dem akuten Lupus erythematosus disseminatus, der Periarthritis nodosa und der Arthritis rheumatoide vorausgehen, folgen oder mit ihnen zu gleicher Zeit auftreten. Das klinische Bild der Polymyositis ist verschiedenartig; aber man beobachtet oft eine proximale "pseudomyopathische" Lokalisation in all diesen Erkrank-

kungen, mit Ausnahme der Periarthritis nodosa, bei der eine mehr lokalisierte, durch den Infarkt bedingte muskuläre Affektion in den Vordergrund tritt. Die Muskelerkrankung kann in bestimmten Fällen das hervorragende Charakteristikum des klinischen Bildes sein. Immerhin kann sie verhältnismässig milde erscheinen, wenn die allgemeinen objektiven und subjektiven Merkmale der in Betracht gezogenen Kollagenkrankheit sehr intensiv sind. Die

Autoren glauben, dass all diese Krankheitsformen Varianten einer einzigen fundamentalen Erkrankung des Bindegewebes sind, die in sehr verschiedenen Formen in Erscheinung treten kann.

An einem Ende der Skala befindet sich die Polymyositis ohne konstitutionelle Symptome, Schmerzen oder Hauterscheinungen, und am andern Ende befindet sich die akute Dermatomyositis mit schweren konstitutionellen Symptomen, begleitet von einer minimalen oder schweren Polymyositis mit einer vorgeschrittenen Kollagenkrankheit, wie z.B. dem Lupus erythematosus oder dem Skleroderma. Es gibt jedoch wahrscheinlich andere Faelle von Polymyositis und zwar toxischer oder metabolischer

Aetiologie, die keine direkte Beziehung zur Kollagengruppe haben. In diese Kategorie mag auch die Entstehung der Polymyositis in Verbindung mit einer boesartigen Erkrankung fallen.

In den meisten Faellen ist das charakteristische histopathologische Bild fuer die Diagnose ausserordentlich nuetzlich; denn die Zeichen der Nekrose der Muskelfasern, der Infiltration und der perivaskulaeren Veraenderungen, sowie auch die Zeichen der Muskelregeneration sind deutlich. Die elektromyographischen Merkmale sind weniger konstant. Die Besserung dieser Faelle durch die Behandlung mit Corticotropin und den Corticosteroiden der Nebenniere ist fuer die Differentialdiagnose von groesster Bedeutung.

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Pathologie des Polymyosites

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Dans son sens le plus général, le terme de myosite désigne tout processus inflammatoire intéressant le tissu musculaire et, d'emblée, deux grands types de myosite peuvent être distingués: dans le premier groupe cette myosite est due à un virus, un parasite, ou n'importe quel agent bactérien; dans le deuxième groupe aucune cause ne peut actuellement être identifiée mais la lésion est présumée inflammatoire en raison de ses caractères histo-pathologiques. C'est ce deuxième groupe que nous aurons en vue ici, pour lequel aussi bien l'étiologie que la pathogénie ne sont à l'heure actuelle connues, que l'on a maintenant l'habitude de classer dans le groupe des maladies dites du collagène, que l'on subdivise enfin en dermatomyosite ou polymyosite suivant que coexistent ou font défaut des signes cutanés.

L'objet de cette étude étant uniquement l'anatomie pathologique des polymyosites, nous ne rappellerons pas les différents aspects cliniques de cette affection envisagés à de multiples reprises dans des études d'ensemble, en particulier l'ouvrage de Adams, Denny-Brown et Pearson⁽¹⁾, notre Rapport avec Jean Gruner et Jean Scherrer à la XXème Réunion neurologique Internationale⁽²⁾, le dernier ouvrage de Walton et Adams⁽³⁾. Nous voudrions insister simplement sur le fait qu'il n'y a pas de corrélation obligatoire entre les différents types cliniques et les lésions constatées à l'examen anatomique: bien au contraire, ces dernières sont relativement univoques et permettent justement l'individualisation comme une entité définie de groupement morbide qui cliniquement pourrait paraître plutôt polymorphe.

Nous allons envisager successivement les

lésions musculaires et les problèmes diagnostiques qu'elles posent.

LESIONS MUSCULAIRES

Elles sont connues à la fois par les examens nécropsiques et par les biopsies musculaires. Nous rappelons, à ce propos, l'intérêt de la biopsie musculaire pour le diagnostic de l'affection du vivant au malade car elle seule permet un diagnostic de certitude. C'est grâce à elle que nous avons pu rassembler en quelques années vingt observations anatomiquement prouvées de polymyosite.

L'aspect macroscopique, à l'autopsie, des muscles atteints de myosite est généralement caractéristique: ces muscles sont en effet de consistance à la fois molle et friable et de coloration gris rosé ou jaunâtre dans les formes récentes, de consistance élastique presque caoutchouteuse dans les formes plus lentes. Ces lésions sont d'étendue variable mais intéressent essentiellement la racine des membres, caractère topographique qui appartient d'ailleurs à toutes les maladies primitives du tissu musculaire.

A l'examen histologique, dans les cas typiques, le diagnostic est fait aisément sur l'association de lésions dégénératives des fibres musculaires et d'une réaction inflammatoire: cette simultanéité dans l'atteinte du parenchyme musculaire proprement dit et de son tissu conjonctif de soutien reste un des meilleurs critères d'identification de la maladie.

L'atteinte musculaire (fig. 1 et 2), proprement dite est toujours sévère mais aucune image élémentaire de dégénérescence n'est spécifique des polymyosites et tous les types classiques peuvent s'observer: dé-



Fig. 1. —
Coloration: hémateine-éosine.
Grossissement: 180 —
Dégénérescences musculaires segmentaires et bariolées dans une polymyosite

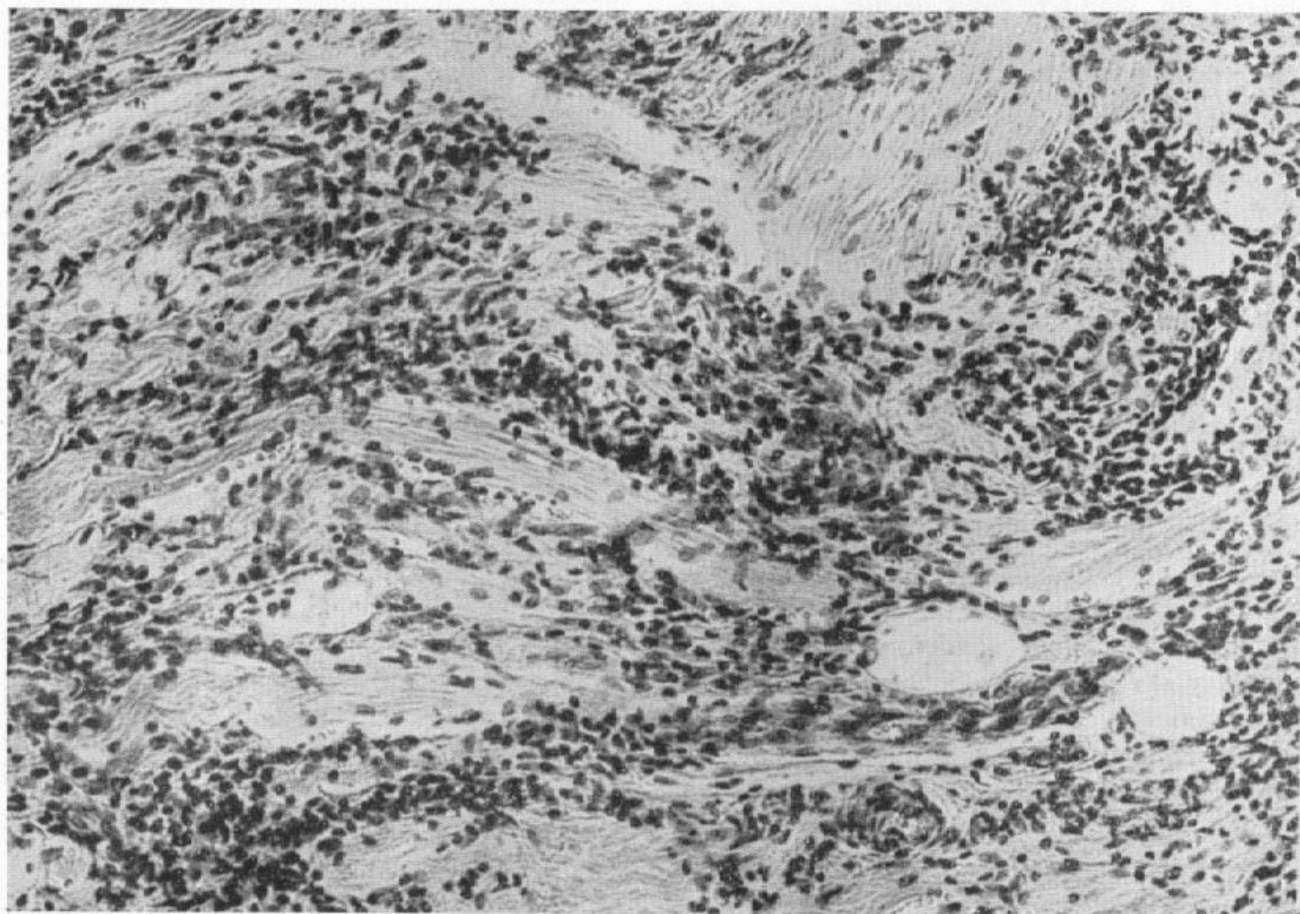


Fig. 2. — Coloration: hémateine-éosine. Grossissement 285 — Atrophie musculaire avec prolifération lymphoréticulaire et sarcolemnique dans une polymyosite

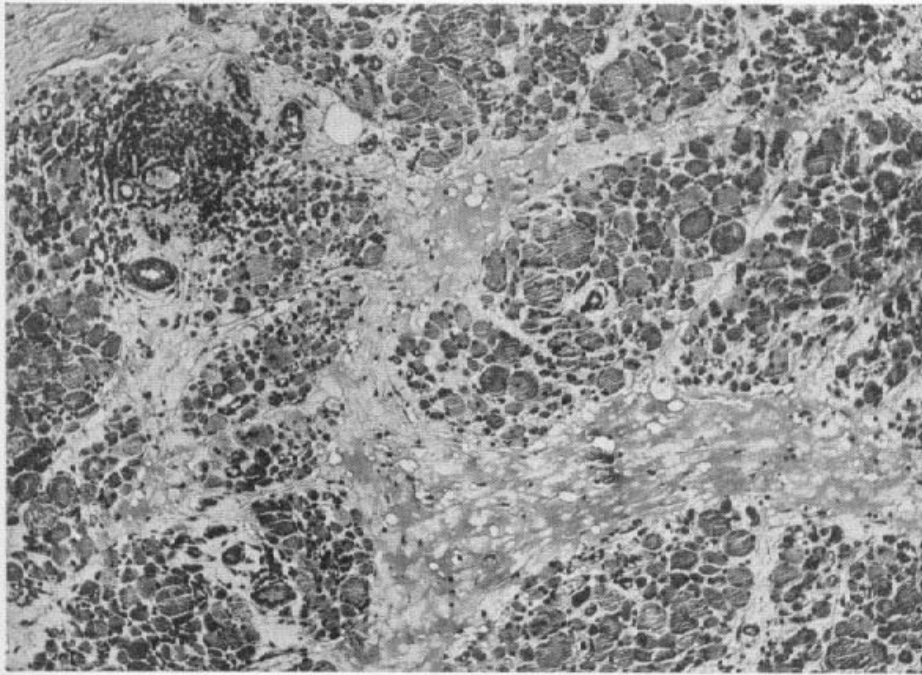


Fig. 3 — Coloration: hémateïne-éosine. Grossissement 180 — Polymyosite: noter l'infiltrat lymphoplasmocytaire à topographie périveineuse et l'œdème interstitiel dissociant les fibres musculaires dont un grand nombre sont en voie de dégénérescence.

générescence granuleuse, hyaline, plus rarement vacuolaire. Par ailleurs, comme dans toutes les dégénérescences de la fibre, les noyaux sarcolemmiques s'hypertrophient et prolifèrent de sorte qu'une disposition en chaîne de ces noyaux ou des images de centralisation au sein d'une fibre encore peu modifiée sont des aspects fréquemment rencontrés mais il est à noter que cette multiplication nucléaire est souvent, en partie du moins, plus apparente que réelle

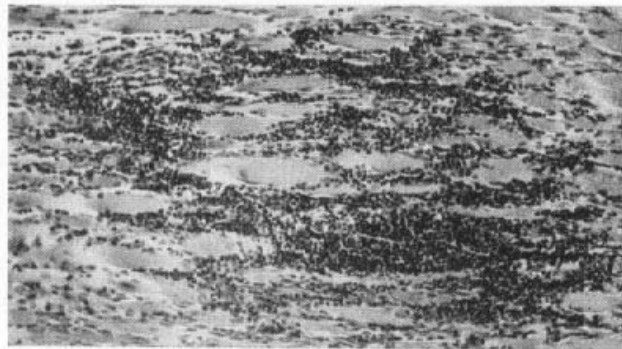


Fig. 5. — Coloration hémateïne-éosine. Grossissement 360 - Polymyosite: infiltrat inflammatoire s'insinuant entre les fibres musculaires.

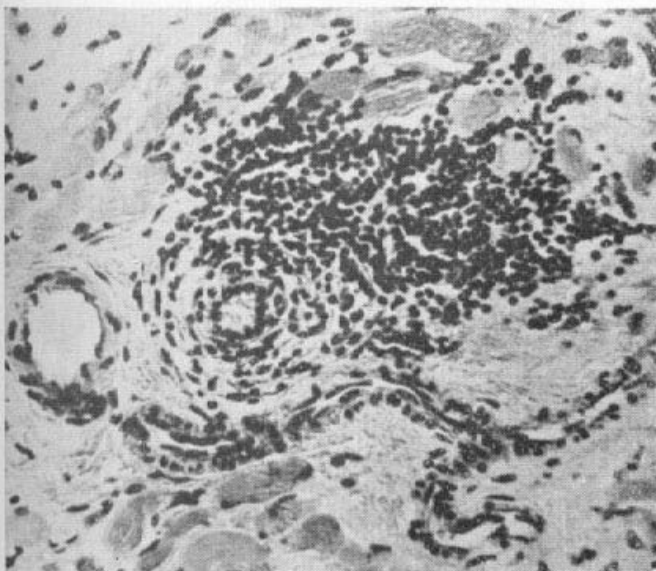


Fig. 4. — Coloration: hémateïne-éosine. Grossissement 200 — Infiltrat à topographie périveineuse dans une polymyosite

parce que majorée par l'atrophie musculaire; il est rare, de plus, que cette prolifération aboutisse à ces aspects symplasmiques qui se rencontrent surtout dans les atrophies neurogènes par dénervation. En outre, Walton et Adams⁽⁸⁾ insistent sur l'inégalité de calibre des fibres avec, présence de fibres nettement hypertrophiques. Enfin, plus importante encore que la morphologie de cette dégénérescence, est la topographie des lésions: en effet, la juxtaposition de fibres indemnes et de fibres segmentairement dégénérées donne à la coupe un aspect bariolé et tacheté très évocateur.

La réaction inflammatoire (fig. 3, 4, et 5) constitue le deuxième élément caractéristique des polymyosites. Cette réaction inflammatoire est à la fois séreuse et cellulaire. L'inflammation séreuse se traduit par la vasodilatation des petits vaisseaux et surtout par des plages d'œdème dissociant les faisceaux musculaires. Il est en principe très caractéristique des formes aiguës mais il peut en fait être retrouvé sur des biopsies de cas évoluant depuis de longs mois, voire des années. Les infiltrats inflammatoires sont formés de lymphocytes mêlés de plasmocytes et d'histiocytes avec, dans les zones nécrotiques, des macrophages. La présence de polynucléaires en petit nombre est habituelle dans les formes de début. Des hématies peuvent s'observer et leur présence exagérée dans certains cas avaient fait parler à Prinzing et Lorenz de polymyosite hémorragique mais qui ne se distingue en fait pratiquement pas de la polymyosite habituelle. Ces infiltrats s'étalent en nappe dans l'endomysium et surtout dans le périmysium. Ils sont plus denses autour des veinules et peuvent gagner les zones où l'atteinte parenchymateuse est moins accentuée. La persistance de ces nodules lymphocytaires ou lymphoplasmocytaires dans les formes traînantes au milieu de faisceaux de fibres pour la plupart dégénérées est très évocatrice et le diagnostic en leur absence est toujours difficile.

A cette description des lésions paren-

chymateuses et inflammatoires caractéristiques des polymyosites nous ajouterons les données suivantes.

Les vaisseaux ne sont pas modifiés mis à part les périvasculaires.

Les nerfs sont également indemnes; en particulier les terminaisons nerveuses, les plaques motrices et les organes sous-neux qui ont été étudiés par Coers et par Woolf⁽²⁾, et dans nos cas par Fardeau⁽³⁾, sont remarquablement conservés alors que le reste du tissu musculaire est durement touché. Ces constatations négatives vont à l'encontre du concept de neuromyosite qui avait été ébauché sur des arguments purement cliniques, par Senator, et qui n'a jamais reçu de confirmation anatomique.

Précisons, enfin, que si les lésions musculaires intéressent essentiellement et presque uniquement la musculature striée, l'atteinte du myocarde n'est pas exceptionnelle sous forme de petits foyers nécrotiques qui prennent volontiers une forme hémorragique.

PROBLEMES DIAGNOSTIQUES

Si l'association de lésions dégénératives et inflammatoires est très caractéristique des polymyosites, l'intensité respective de ces lésions peut varier; c'est alors que certains diagnostics différentiels doivent être envisagés.

Le premier problème qui se pose habituellement est le diagnostic avec une *atro-*

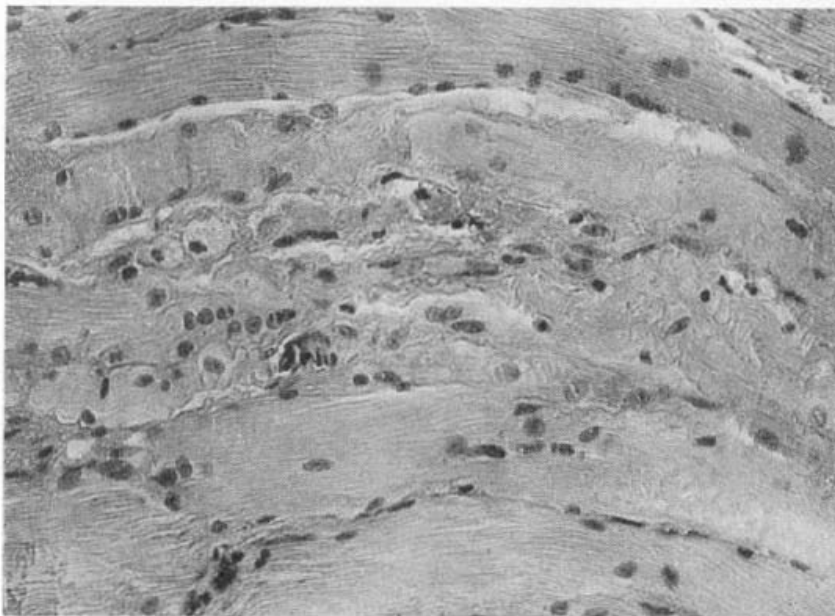


Fig. 6. — Coloration: hématoxyne-éosine. Grossissement 360. Myopathie tardive du type Nevin: nécrose localisée des fibres musculaires avec corps granulo-grasieux et sans réaction inflammatoire interstitielle.

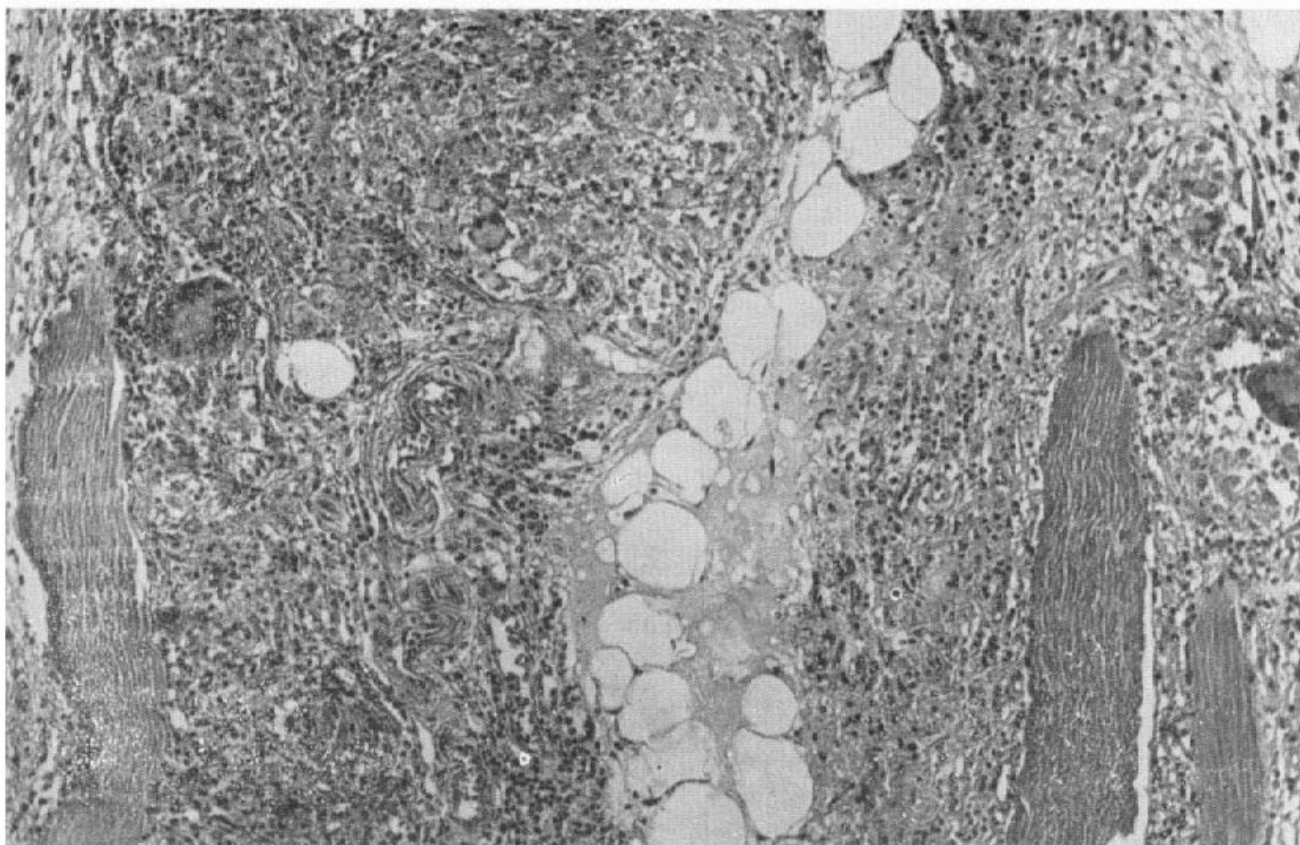
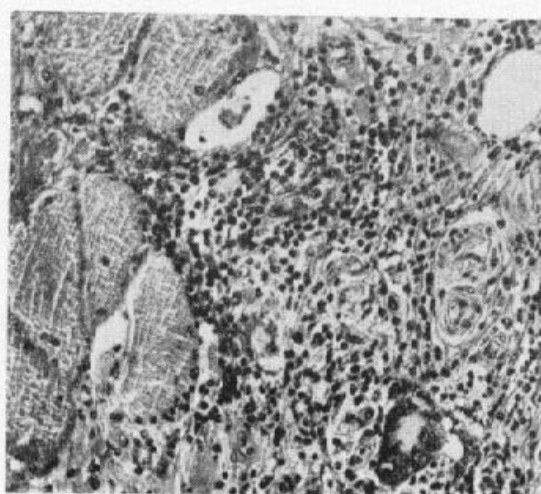


Fig. 7. — Coloration: hémateïne-éosine. Grossissement 135. Sarcoïdose musculaire: prolifération lymphoplasmocytaire et réticulaire avec présence d'éléments plasmodiaux multinucléés; noter l'aspect normal des quelques fibres musculaires épargnées par cette myosite interstitielle.

phie neurogène. Ce diagnostic différentiel repose sur trois arguments. C'est d'abord la topographie des dégénérescences qui dans l'atrophie neurogène intéresse toutes les fibres musculaires dépendant de la même grappe neuromyotique et sur toute leur longueur alors qu'à l'inverse dans les processus myogènes en général, et les myosites en particulier, les dégénérescences sont disséminées et segmentaires; une certaine prédisposition régionale, rappelant une topographie fasciculaire, a bien été signalée, par Walton et Adams⁽⁸⁾, dans certaines myosites mais dans notre expérience personnelle nous ne l'avons pratiquement pas rencontrée et l'argument topographique reste pour nous très important. C'est, par ailleurs, le type de la dégénérescence: dans l'atrophie neurogène,

en effet, l'on observe au mieux ces condensations de noyaux au niveau de fibres dégénérées qui réalisent des aspects symplasmiques rappelant une cellule géante; de tels aspects sont très rares, avons nous déjà dit,

Fig. 8. — Coloration: hémateïne-éosine. Grossissement 200 — Même aspect que la figure précédente mais cette fois sur une section transversale du muscle



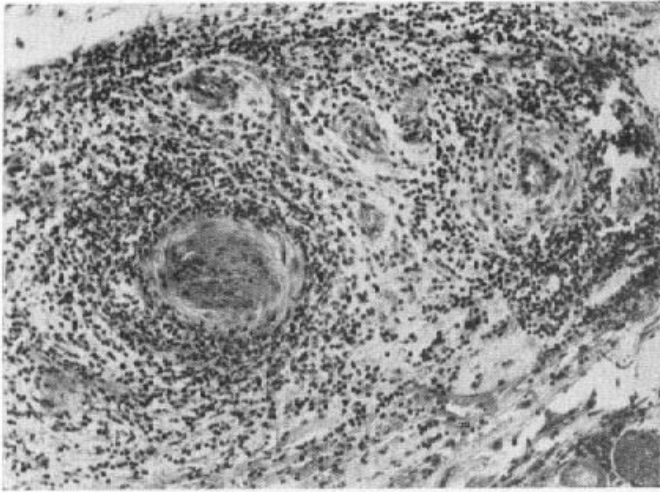


Fig. 9. — Coloration: hématoxyline-éosine. Grossissement 600 - Lésions artériolaires caractéristiques d'une périartérite noueuse dans une biopsie musculaire.

dans les polymyosites où les noyaux sarcolemmiques sont même gonflés et clairs et non pas rétractés et denses comme dans les dénervations. C'est enfin, l'absence de réaction inflammatoire notable.

Une fois le diagnostic de processus myogène porté, un deuxième problème se pose, c'est celui de sa nature et, schématiquement, trois types d'affection musculaire peuvent être envisagés: 1^o) les polymyosites que nous venons de voir et qui frappent simultanément les fibres musculaires et le tissu interstitiel; 2^o) les affections proprement parenchymateuses du tissu musculaire, c'est-

à-dire les dystrophies musculaires progressives; 3^o) les affections purement inflammatoires, c'est-à-dire les myosites interstitielles.

Le diagnostic d'une *atrophie myogène dystrophique*, c'est-à-dire d'une myopathie au sens étroit du mot, repose sur trois critères: la topographie bariolée des lésions qui appartient à tous les processus myogènes, l'absence de réaction inflammatoire notable, la présence de malformations musculaires (inégalités de calibre avec hypertrophie des fibres, centralisations nucléaires, images annulaires de Heidenhain, etc...); ces deux derniers critères distinguent les dystrophies des polymyosites. Habituellement le diagnostic est donc facile mais certaines observations posent un problème plus délicat dont nous voudrions dire quelques mots. Il s'agit de ces faits qui avaient été rassemblés en 1936 par Nevin sous le nom de myopathie progressive tardive et plus tard, en 1951, par Shy et Mc Eachern sous le nom de dystrophie musculaire de la ménopause: dans tous ces cas la biopsie musculaire montrait des lésions anatomiques très spéciales faites de foyers nécrotiques disséminés avec présence de macrophages mais sans infiltrats (fig. 6); cette lésion se distinguait donc des dystrophies musculaires progressives par l'absence complète de tout élément malformatif et des polymyosites habituelles par l'absence de réaction inflammatoire. La place de cette

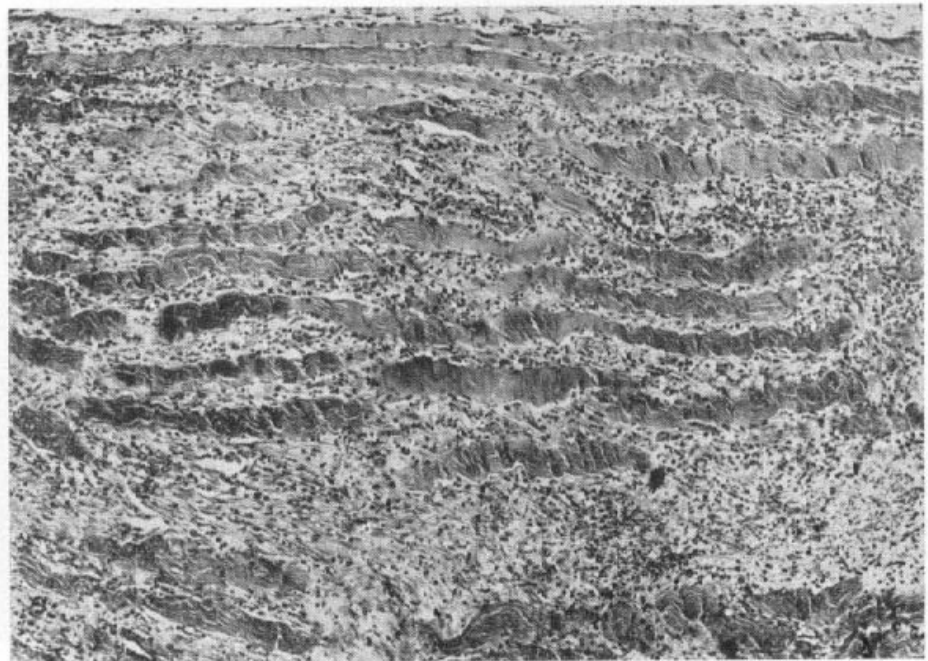


Fig. 10. — Coloration: hématoxyline-éosine. Grossissement 120. Même aspect que la figure précédente: noter l'intense prolifération interstitielle.

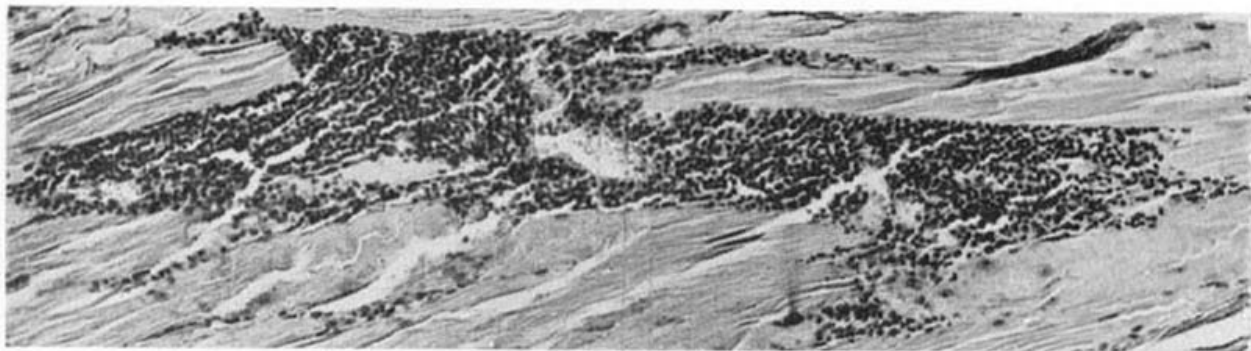


Fig. 11. — Coloration: hémateïne-éosine. Grossissement 110.
Lymphorrhage dans une myasthénie.

entité nosologique a été très discutée. Pour Nevin, qui l'a décrite, il s'agissait d'une variété de myopathie au sens étroit du mot, c'est-à-dire d'un type spécial de dystrophie musculaire progressive, alors que d'autres comme Eaton, Adams et ses collaborateurs la classait dans le groupe des myosites. A propos d'une observation personnelle (4), nous avons déjà dit que cette dernière interprétation nous paraissait la plus vraisemblable pour les raisons suivantes; le mode évolutif est beaucoup plus rapide que dans les myopathies et très comparable à celui des myosites, on y peut observer des troubles de la déglutition oesophagienne qui

sont très fréquents dans les polymyosites alors qu'ils font habituellement défaut dans les myopathies, ces lésions nécrotiques font partie du tableau histologique des polymyosites alors qu'on ne les observe pas dans les dystrophies musculaires progressives, l'hormonothérapie cortico-surrénalienne enfin est remarquablement efficace (ayant permis par exemple la guérison complète de notre malade) et cette action thérapeutique rapproche beaucoup plus ces faits d'une affection inflammatoire que d'une affection dystrophique du muscle, où elle s'est montrée jusqu'à présent inefficace.

Il reste enfin un dernier problème, c'est

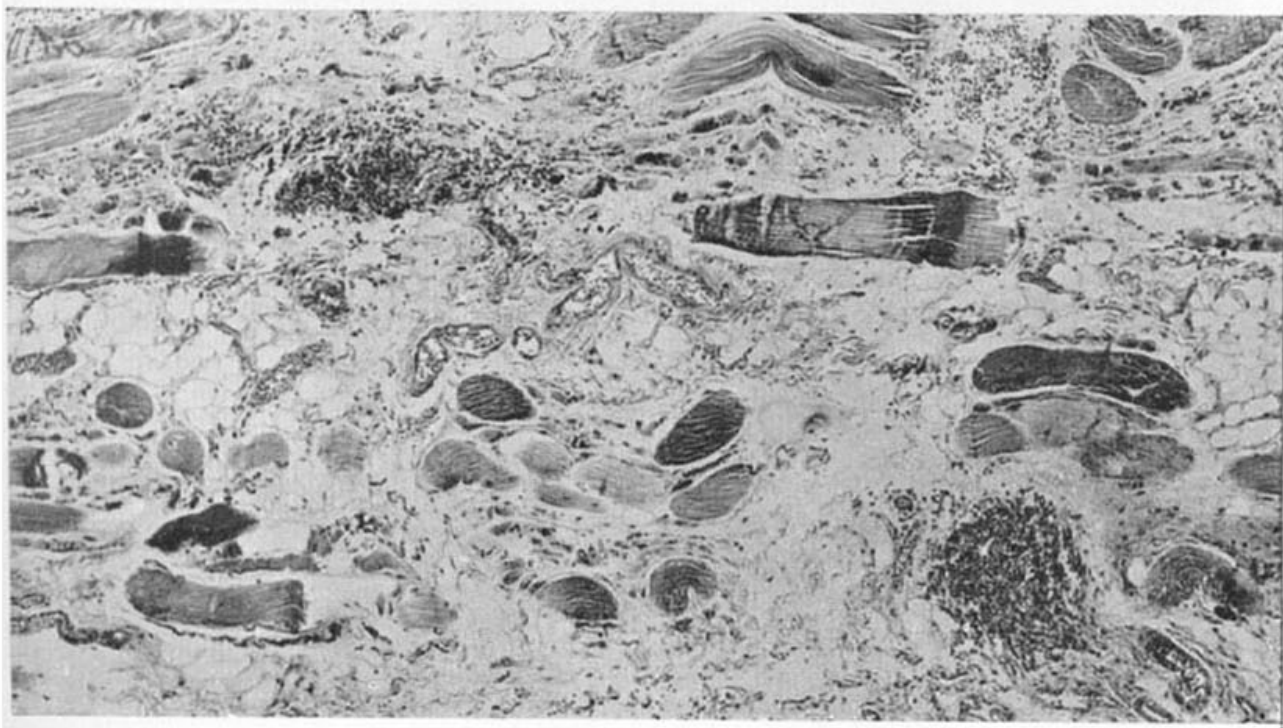


Fig. 12. — Coloration: hémateïne-éosine. Grossissement 60.
Infiltrats et atrophie musculaire dans une myasthénie.

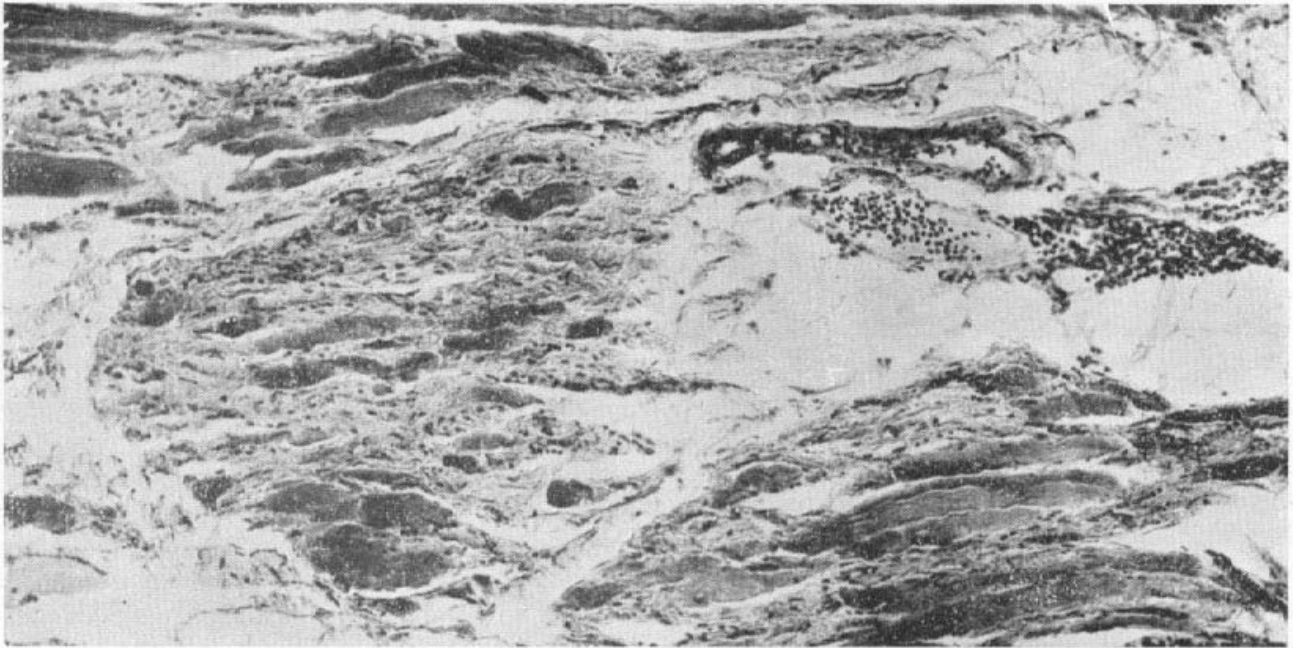


Fig. 13. — Coloration: hémateine-éosine. Grossissement 110.
Infiltrats et atrophie musculaire dans une myasthénie.

celui des *myosites interstitielles*, c'est-à-dire des maladies inflammatoires touchant le tissu conjonctif du muscle mais épargnant les fibres musculaires proprement dites ou tout au moins ne les lésant que secondairement,

au prorata de leur envahissement par le processus inflammatoire interstitiel. De nombreuses affections peuvent réaliser un tel tableau mais, dans notre expérience personnelle, nous l'avons rencontrée dans les

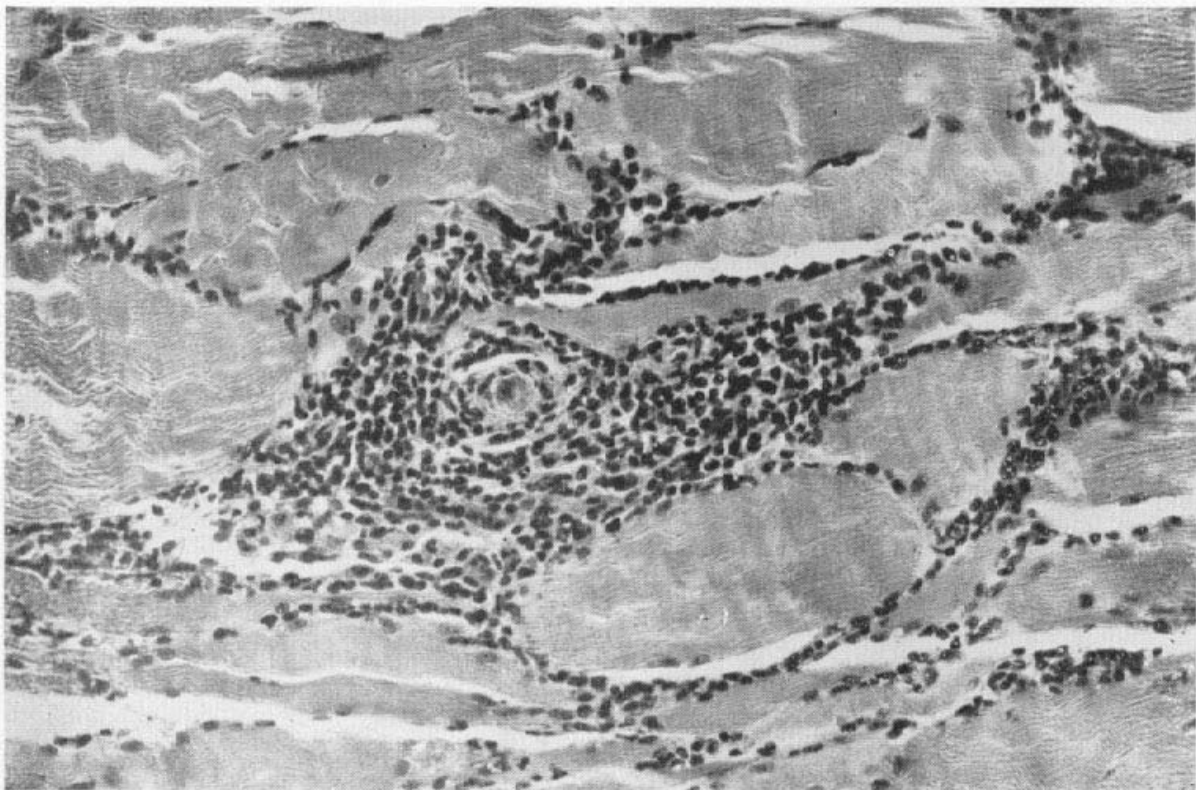


Fig. 14. — Coloration: hémateine-éosine. Grossissement 190. — Infiltrat péri-vasculaire dans une macroglobulinémie de Waldenström.

éventualités suivantes. Dans la sarcoïdose musculaire d'abord à propos d'une observation (5) dont le tableau clinique était celui d'une polymyosite typique et où seule la biopsie musculaire a permis de montrer des altérations caractéristiques de la maladie de Besnier-Boeck-Schaumann (fig. 7 et 8). Nous avons rencontrée également des lésions de myosite interstitielle dans les affections voisines des polymyosites qui appartiennent également aux maladies dites du collagène, la périartérite noueuse en particulier (fig. 9 et 10); il faut bien connaître l'existence de ces réactions inflammatoires du tissu musculaire pour ne pas les interpréter nécessairement comme une polymyosite associée et nous pensons, personnellement, que nombre de formes dites transitionnelles entre ces diverses entités

ne reposent que sur pareilles erreurs d'interprétation. Dans la myasthénie, également, l'on peut observer des infiltrats, les classiques lymphorrhages de Buzzard (fig. 11), mais qui peuvent être associés comme nous l'avons vu dans deux observations (fig. 12 et 13) à des lésions dégénératives des fibres musculaires posant sur le terrain purement pathologique un problème diagnostique très difficile. Il nous est arrivé enfin de rencontrer également de tels infiltrats (fig. 14) dans une macroglobulinémie de Waldenström (7).

Pour terminer, nous voudrions encore insister sur le fait que les lésions musculaires des polymyosites sont à la fois parenchymateuses et interstitielles, cette association restant le meilleur critère diagnostique de la maladie.

RESUME

Les lésions musculaires qui caractérisent les polymyosites sont à la fois parenchymateuses et interstitielles, cette association constituant le meilleur critère diagnostique de ce groupe morbide dont les lésions anatomiques sont relativement univoques. Les auteurs insistent sur l'intérêt considérable des biopsies musculaires qui leur ont permis d'authentifier anatomiquement vingt cas de polymyosites en quelques années. L'association de lésions dégénératives des fibres musculaires et d'une réaction inflammatoire interstitielle constitue la signature histo-pathologique des polymyosites.

L'atteinte sévère de la fibre musculaire réalise les divers types élémentaires de la dégénérescence. Plus importante que la morphologie de cette dégénérescence est la topographie des lésions, la juxtaposition de fibres indemnes et de fibres segmentairement dégénérées donnant à la coupe un aspect *bariolé* et *tacheté très évocateur*.

La réaction inflammatoire, deuxième élément caractéristique des polymyosites est à la fois séreuse et cellulaire. L'inflammation séreuse se traduit par des plages d'œdème dissociant les faisceaux musculaires et la vaso-dilatation des petits vaisseaux. Les infiltrats inflammatoires sont formés de

lymphocytes mêlés de plasmocytes et d'histiocytes avec des macrophages dans les zones nécrotiques, infiltrats s'étalant en nappe dans l'endomysium et surtout le péri-myosium, plus denses au niveau des veinules. Deux caractères négatifs importants: l'absence de modifications des vaisseaux (mis à part les périvascularites) et l'intégrité des nerfs, des terminaisons nerveuses, des plaques motrices et des organes sous-neuraux si bien que le concept de neuro-myosite (Senator) attend encore sa confirmation anatomique.

L'intensité respective des lésions dégénératives et des lésions inflammatoires, dont l'association est caractéristique des polymyosites, peut varier; c'est alors que certains diagnostics différentiels peuvent se poser.

L'atrophie neurogène a pour elle la topographie des dégénérescences qui frappent toutes les fibres dépendant d'une même grappe neuromyotique et cela sur toute leur longueur. L'absence de réaction inflammatoire notable est enfin la règle dans l'atrophie neurogène.

Une fois, le diagnostic de processus myogène porté, le diagnostic est à faire avec l'atrophie des dystrophies musculaires (myopathies) et les auteurs en précisent les

caractères différentiels. Ils pensent avec EATON, ADAMS que la myopathie progressive tardive de NEVIN doit être classée dans le groupe des myosites.

Le diagnostic est également à faire avec les myosites interstitielles (où le processus inflammatoire épargne les fibres musculaires proprement dites) et les auteurs n'ont retrouvé pareil tableau que dans la sarcoïdose musculaire et la périartérite noueuse. Dans la myasthénie il est classique de re-

lever la présence d'infiltrats (lymphorrhages de Buzzard) mais dans 2 observations les auteurs ont noté également l'association de lésions dégénératives des fibres musculaires. Des infiltrats périvasculaires ont été également observés par eux dans un cas de macroglobulinémie de Waldenström.

Les auteurs illustrent ce travail de quatorze microphotographies provenant de leur collection personnelle.

SUMMARY

The muscular lesions characteristic in polymyositis are at the same time parenchymatose and interstitial, this combination constitutes the best criterium for diagnosing this morbid group where the anatomic lesions are relatively various and sundry.

The authors insist on the importance of the muscular biopsies which have allowed them to verify anatomically twenty cases of polymyositis during several years. The combination of degenerative lesions of the muscular fibers and an interstitial inflammatory reaction constitute the histopathological sign of polymyositis.

The severe attack of the muscular fiber brings about different elementary types of degeneration.

More important than the morphology of this degeneration is the topography of the lesions, the juxtaposition of untouched fibers and the fiber partially degenerated gives to the cross sections a conglomerated and a spotty aspect which is very peculiar.

The inflammatory reaction the second characteristic of polymyositis is at the same time serous and cellular. The serous inflammation is evident by the zones of edema cut off the muscular fasciculus and the vasodilatation of the little vessels. The inflammatory infiltration is formed by lymphocytes mixed with plasmocytes and histiocytes with macrophages in the necrotic zones.

Infiltrations which spread as layers into the endomysium and above all into the perimysium, more dense to the levels of the venules.

Two important negative features: the absence of modifications of the vessels excepting the perivascularitis and the integrity of the nerves, of the nervous endings, of the motor plaques and of subneuronal organs so that the concept of neuromyositis (Senator) is still waiting for its anatomical confirmation.

The respective intensity of the degenerative lesions and the inflammatory ones, which characteristically accompany polymyositis can be variable, then it is when certain differential diagnosis can be posed. The neurogenic atrophy has the topography of the degenerations that strike all the fibers belonging to the same neuromyonic bunch and this covers it entirely. The absence of noticeable inflammatory reaction is the rule in neurogenic atrophy.

Once the diagnosis of the myogenic process is given, the next step is a diagnosis related to the atrophy of the muscular dystrophies (myopathies) the authors point out its differential characteristic. They think along with Eaton and Adams that the delayed myopathic progressive of Nevin ought to be classified in this group of myositis.

Another differential diagnosis should also be done with the myositis interstitiale (where inflammatory process leaves untouched the muscular fibres themselves) and the authors didn't find any clinical pictures alike except in muscular sarcoidosis and the periarteritis nodosa. In the myasthenia it is a general rule to find the presence of

ZUSAMMENFASSUNG

Die Veraenderungen in den Muskeln, die die Polymyositiden charakterisieren, sind zur gleichen Zeit parenchymatoes und interstitiell; und diese Assoziierung stellt das beste diagnostische Kriterium dieser Krankheitsgruppe dar, bei denen die anatomischen Veraenderungen verheltnismaessing eindeutig sind. Die Autoren bestehen auf das erhebliche Interesse fuer die Muskelbiopsien, welche ihnen erlaubt haben, in wenigen Jahren zwanzig Faelle von Polymyositis anatomisch zu identifizieren. Die Assoziierung von degenerativen Veraenderungen der Muskelfasern und einer entzuendlichen interstitiellen Reaktion sind das histo-pathologische Zeichen der Polymyositiden.

Die schwere Erkrankung der Muskelfaser geht ueber verschiedene elementaere Etappen der Degeneration. Wichtiger als die Morphologie dieser Degeneration ist die Topographie der Laesionen, das Nebeneinanderbestehen von intakten Fasern und Fasern, die segmentweise degeneriert sind und im Schnitt einen bunten y fleckigen sehr eindrucksvollen Anblick bieten.

Die entzuendliche Reaktion, das zweite charakteristische Element der Polymyositis, ist sowohl seroes als auch zellulaer. Die seroese Entzuendung zeigt sich durch seroese Ansammlungen, die die Muskelbuendel auseinanderreissen, und die Erweiterung der kleinen Gefaesse.

Die entzuendlichen Infiltrate bestehen aus Lymphozyten, Plasmazellen und Histiozyten mit Makrophagen inden nekrotischen Zonen. Die Infiltrate breiten sich flaechenfoermig im Endomysium und vor allem im Perimysium aus und sind am dichtesten in der Naeh der Venulen. Zwei wichtige negative Eigenschaften: Das Nichtvorhandensein von Gefaessveraenderungen (ausser den Perivascularitiden) und die Unversehrtheit der Nerven, der Nervenendigungen, der motorischen Endplatten und der sub-

neuralen Organe, sodass der Begriff der Neuro-Myositis (Senator) noch seine anatomische Bestaetigung erwartet.

Sowohl die besondere Intensitaet der degenerativen als auch die der entzuendlichen Veraenderungen, deren Assoziierung charakteristisch fuer die Polymyositiden ist, koennen variieren; dadurch koennen gewisse Differentialdiagnosen in Frage kommen.

Fuer die neurogene Atrophie spricht die Topographie der Degenerationen, die alle von einer und derselben myoneuralen Gruppe abhaengigen Muskelfasern in ihrer ganzen Laenge trifft. Endlich ist das Nichtvorhandensein bemerkenswerter entzuendlicher Veraenderungen die Regel bei der neurogenen Atrophie.

Sobald man die Diagnose eines myogenen Prozesses gestellt hat, muss man die Differentialdiagnose mit den Atrophien der muskulaeren Dystrophien (Myopathien) stellen und die Autoren praezisieren die unterschiedlichen Charaktere. Sie sind mit Eaton und Adams der Meinung, dass die Myopathia progressiva tarda von Nevin in die Gruppe der Myositiden eingereiht werden muss.

Man muss ebenfalls die Differentialdiagnose mit der interstitiellen Myositis stellen (bei welcher der entzuendliche Prozess die eigentlichen Muskelfasern auseinanderdrueckt); und die Autoren haben ein aehnliches Bild nur beim der muskulaeren Sarkoidosis und bei der Periarteritis nodosa wiedergefunden.

Bei der Myasthenie ist es klassisch, die Anwesenheit von Infiltraten (den Lymphorrhagien von Buzzard) hervorzuheben, aber bei zwei Faellen haben die Autoren ebenfalls die Assoziierung mit degenerativen Veraenderungen der Muskelfasern beobachtet. Sie haben auch perivaskulaere Infiltrate bei einem Fasll von Waldenstromscher Makroglobulinaemie beobachtet.

Die Autoren illustrieren diese Arbeit durch 14 Mikrophotographien aus ihrer persoenlichen Sammlung.

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The Clinical Picture and Treatment of Polymyositis

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It is difficult in a short account to do justice to the remarkable pleomorphism which characterizes the clinical presentation of polymyositis. Extreme variability is found in the symptomatology, objective findings and natural history of the condition. However, certain constellations of symptoms and signs, frequently found together, allow division of cases of the disease into several clinical sub-groups.

CLINICAL CLASSIFICATION

Walton and Adams (1958), on the basis of their personal experience of forty cases, divided polymyositis into four groups:—

Group I — In which the disease process is confined to the muscles and which may be called simply, polymyositis. Included here are acute, subacute and chronic cases occurring at all ages.

Group II — Here muscular involvement dominates the clinical picture but also present, at least at some stage in the evolution of the condition, is evidence either of skin changes or of a "collagen" disease — but these features are always unobtrusive.

Group III — Instead of prominent muscular involvement these cases are characterised by florid skin changes (dermatomyositis) or severe "collagen" disease with muscular weakness of lesser degree.

Group IV — In this category are those cases in which a myopathic process is associated with malignant disease. Hence, inclusion of cases in this arbitrary category depends upon demonstration of malignancy;

otherwise they may closely resemble other in each of the three other groups.

INCIDENCE

No true estimate of racial or geographical incidence of the disease is at present possible; as well as appearing in Anglo-Saxon and Mediterranean stock (Eaton, 1954; van Bogaert et al., 1955) the disorder has been reported in South America (Mussa et al., 1958; Garzón et al., 1959) and more recently in Africa in the negro (Barnard et al., 1960). The disease occurs at almost any age. Garcin et al. (1955) suggest that three and seventy-seven should be the lower and upper limits, but Wedgwood et al. (1953) reported the development of the disease in childhood as early as the age of two years, and Walton and Adams (1958) in the first year. Walton and Adams found the disease to be twice as frequent in females as in males. Cases associated with malignant disease are, however, much more equally distributed, being mainly confined to patients in middle age. Florid dermatomyositis and severe "collagen" disease with secondary muscle involvement are uncommon in childhood.

CLINICAL FEATURES

a. Onset

The previous history obtained from patients with polymyositis and from their relatives is usually unrevealing. A history of allergic disorders or of "collagen" diseases is unusual.

Among precipitating factors, an antecedent febrile illness (Ford, 1952), various infections and trauma (van Bogaert et al., 1955), acute exanthemata (Lingenfelter, 1940; Lane, 1940; Selander, 1950) pneumonitis (Mills and Matthews, 1956) and numerous other infective disorders (Garcin et al., 1955) have been invoked, but no clear relationship has emerged. No physical or toxic agents appear to be of any importance, though the facial eruption in dermatomyositis often appears following exposure to the sun (Wedgwood et al., 1953; Garcin et al., 1955) and photosensitivity is common at all stages.

As Sheard (1951), Wedgwood et al. (1953) and Midana and Léone (1953) among others, have pointed out, the development of polymyositis may follow sulphonamide therapy, or if pre-existing, be made worse by such therapy. Although endocrine disorders such as hyperthyroidism or pituitary and adrenal dysfunction, may be associated with myopathy, there is no real evidence to suggest that endocrine diseases bear any causal relationship to polymyositis.

The relationship to malignant disease is at times tenuous and ill-defined and its basis obscure. Christianson et al. (1956) deny that the relationship is anything but fortuitous, since both conditions occur in similar age groups. However, Schuermann (1954) estimated that the incidence of malignancy is five times greater than that expected on a chance basis, and the relationship is now generally accepted.

b. Clinical manifestations in cases of the different groups

Group I Polymyositis, acute, subacute and chronic

1. Acute cases

Symptoms of constitutional disturbance, fever, malaise, sore throat and dysphagia, together with severe muscular pains and swollen, painful joints are prominent. A history of production of dark urine may be given and the urine may be found to contain myoglobin. No definite skin chan-

ges are present, but oedema of the limbs, or of the face (particularly periorbital) may be evident. In severely affected cases, the associated prostration may make demonstration of muscular weakness difficult. Where systemic illness is less severe, the presence of severe, global weakness of proximal muscles of the limbs, neck and in certain instances of face and jaw, without atrophy is striking, and the muscles are usually markedly tender.

Other features often present are gross weight loss, splenomegaly, hepatomegaly and generalised lymphadenopathy. These features are not, however, confined to this group, as they also occur in some cases of subacute polymyositis and in acute derma-



Fig. 1

tomyositis (Wilson, 1954; Garcin et al., 1955). Signs of cardiac involvement other than electrocardiographic evidence of myocardial involvement are usually slight or absent. Renal involvement, however, is common and clinical evidence of uraemia and death from renal failure is seen in cases with massive myoglobinuria, when renal tubular block by myoglobin may be produced. The erythrocyte sedimentation rate is almost always raised, the level of serum enzymes such as the transaminases and aldolase is grossly elevated and the electromyogram and muscle biopsy will confirm the diagnosis.

Differential diagnosis

Acute polymyositis must be differentiated from paroxysmal paralytic myoglobinuria, a syndrome recently reviewed by Korein et al. (1959). In cases of the latter condition, in which repeated attacks occur in relation to exercise, confusion should not arise. But when the disorder affects children, as an acute severe illness, often precipitated by infection, the resemblance to acute polymyositis may be very striking, especially when subcutaneous oedema and cutaneous erythema accompany the attack (Acheson and McAlpine, 1953). The presence or absence of inflammatory infiltrates in a muscle biopsy may provide the only means of distinction, for the other muscular lesions are common to both conditions.

In infective myositic diseases such as Bornholm disease and parasitic myositis (e.g. trichiniasis), the very acute onset, the prominence of pain and the absence of muscular weakness should allow differentiation from polymyositis. Acute anterior poliomyelitis and the Guillain-Barre syndrome present with a rapidity of onset never seen in polymyositis and sensory signs are invariable in the radicular syndrome. Sensory symptoms and signs, abdominal pain, confusion and urinary changes serve to differentiate the acute polyneuropathy of porphyria. However, the presence of coproporphyrin in the urine in dermatomyositis has been reported by Novelletto and Sollini (1958), and by Teodoresco and Dumitriu (1959) while dermatomyositis in

association with a fully developed non-familial porphyria is reported by Borda and Stringa (1958).

2. Subacute and chronic cases

In contrast to the acute cases, these patients rarely experience constitutional symptoms and evidence of muscular involvement predominates. Thus, complaints of weakness in the legs, difficulty in climbing stairs or difficulty in walking are the presenting features, initial weakness of the upper limbs being less frequent. Alternatively, aching pains in the involved muscles may be the most distressing feature while difficulty in swallowing is an early and common complaint. As the disease

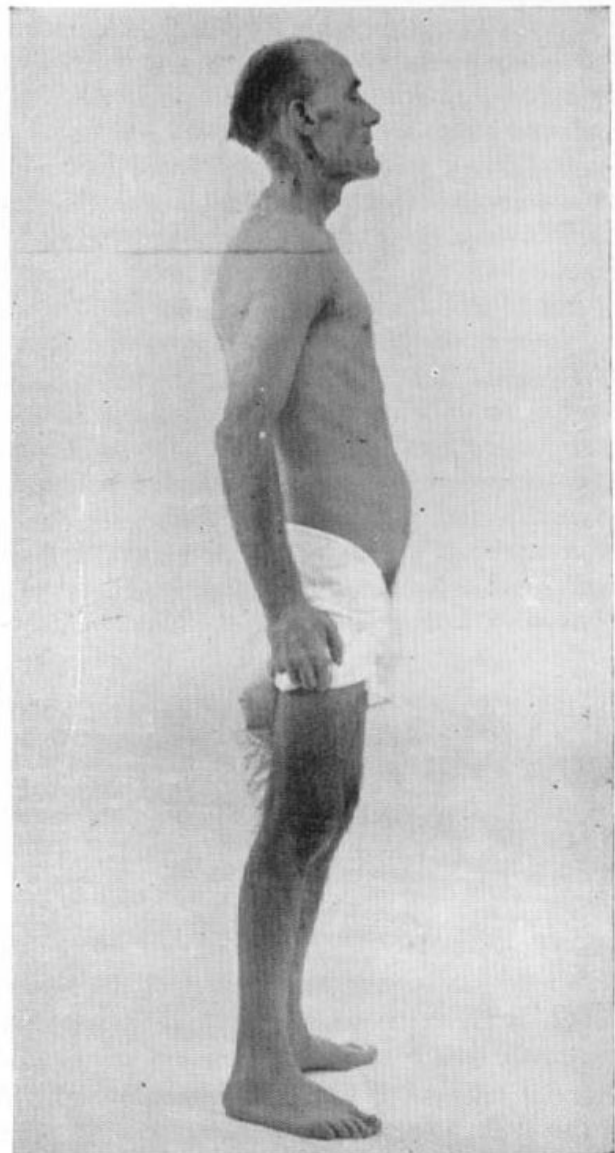


Fig. 2

progresses, involvement of shoulder as well as pelvic girdle muscles is frequent, and facial weakness, though often slight, is not uncommon.

Myasthenic features occur in a proportion of patients, though this feature is not solely confined to this group. There may be rapidly progressive fatigability with activity. Muscular weakness then becomes increasingly severe as the day progresses, and shows some improvement with prostigmine.

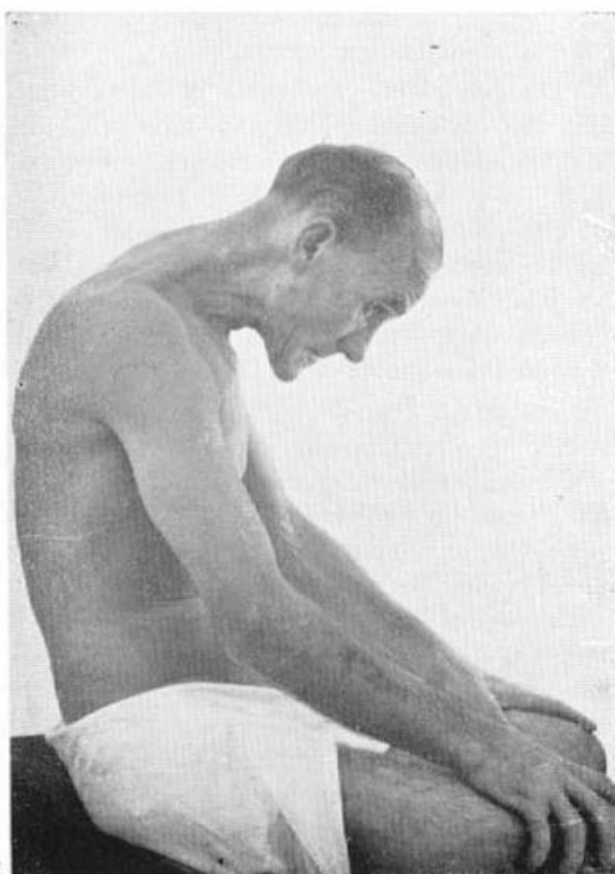
Evidence of constitutional disturbance, seen sometimes in the subacute and never in the chronic cases, is a good deal less frequent and severe than in the acute group. However, fever, splenomegaly, hepatomegaly and lymphadenopathy are rarely found. The Raynaud phenomenon is occasionally seen but skin changes are by definition absent. Dysphagia in such cases is usually due to pharyngeal muscle involvement.

In many patients, evidence of muscular involvement is seen in the waddling gait, accentuated lumbar lordosis and the use of the hands in arising from a supine position. Concurrent weakness in shoulder girdle muscles may be prominent. In chronic cases the lower limbs are most often first affected though cases with initial shoulder girdle involvement have been reported (Biernard, 1948; van Bogaert et al., 1955). Usually muscular weakness is proximal, at least initially (Figs. 1 and 2), though progressive cases may demonstrate distal spread. However, there was predominantly distal muscle involvement in one of Eaton's (1954) cases and chronic distal polymyositis has been described by Denny-Brown (1960). Although weakness is almost bilateral and symmetrical, it was asymmetrical and mainly unilateral in van der Lugt's (1952) case. Many patients also demonstrate marked involvement of the sterno-mastoids and anterior muscles of the neck, and frequently the neck extensors also (Fig. 3). Other muscles sometimes affected are the paravertebral muscles, abdominal muscles and in certain severe cases the intercostals and diaphragm. Facial involvement and much more rarely affection of external ocular muscles may be present. Where facial weakness is evident,

the muscles of facial expression and mastication may be attacked, while diplopia and partial or complete external ophthalmoplegia may rarely be produced by ocular muscle involvement.

Muscular wasting, considerable in some cases, is surprisingly mild in others and out of proportion to the degree of weakness present. Pseudohypertrophy, particularly of calf muscles is not uncommon, resembling, by virtue of the sharply defined margins and firm doughy consistency of the affected muscle, that sometimes seen in progressive muscular dystrophy.

It is generally accepted that severe weakness and wasting of certain muscles with virtual sparing of others adjacent, is characteristic of progressive muscular dystrophy, in contrast to the more or less equal involvement of all adjacent groups in polymyositis. That this provides a useful means of distinguishing the two conditions.



Figs. 1-3. — A case of subacute polymyositis with considerable weakness, but comparatively little atrophy, of proximal limb muscles, and particularly of posterior neck muscles

is, however, not always true. Rare cases of polymyositis may demonstrate remarkably selective weakness and atrophy of some, with relative sparing of other adjacent muscles. One of us (J.N.W.) made a confident clinical diagnosis of limb-girdle dystrophy in a recent case because of this feature and the diagnosis of polymyositis was confirmed unequivocally by muscle biopsy and by the patient's response to treatment. The true diagnosis may only be suspected when there is evidence of marked affection of the neck muscles, rapid progression, or remission, features which are out of keeping with the natural history of the hereditary condition.

Tenderness of involved muscles, present in a minority of patients, is not necessarily restricted to those who complain of muscular pain. Reflex changes are variable, the deep tendon reflexes being quite often normal, while widespread depression of the jerks may be present in other patients. On other occasions, for no apparent reason, they are remarkably brisk.

Contracture formation is a feature of some chronic cases of polymyositis (chronic myositis fibrosa), in advanced chronic cases bony atrophy with decalcification, particularly in the shafts of long bones, may be seen. Subcutaneous and intramuscular calcification occasionally occurs but is much more frequent in cases with skin changes (Groups II and III).

A fluctuant course with distinct exacerbations and remissions may characterize the illness, or else deterioration for a short period can be followed by arrest. Alternatively, slow, gradual progression over several years may occur, very reminiscent of the course of muscular dystrophy. This latter mode of progression is probably more common in middle-aged or elderly females (Shy and McEachern, 1951) but as yet no definite relationship between clinical picture and prognosis has emerged. Probably the outlook is generally better in children and young adults in whom long-lasting remissions may occur. Such cases, as Natrass (1954) pointed out, probably account for most reports in past years of recovery from "muscular dystrophy".

However, in many of the slowly progres-

sive cases the ESR and the serum proteins are normal and the electromyogram shows changes equally compatible with a diagnosis of progressive muscular dystrophy. Diagnosis may then rest upon muscle biopsy and even this can be negative. If there is then no clinical response to steroids it may be difficult to justify the clinical diagnosis of polymyositis. These cases, which resemble the familial myosclerosis of Löwenthal (1954) and the senile myosclerosis mentioned by Garcin et al. (1955) are at present difficult to classify accurately, and there may be, as Rowland (1958) has pointed out, no way of distinguishing these from isolated late cases of "limb-girdle dystrophy" (Walton and Natrass, 1954).

Differential diagnosis

The diagnostic problems posed by subacute and chronic polymyositis have been emphasized recently by Heathfield and Williams (1960). Cases without skin involvement are rare in infancy and early childhood, but when they do occur they may be confused with other causes of the amyotonia congenita syndrome (Walton, 1956) and muscle biopsy is often necessary for diagnosis. Polymyositis in childhood and adult life must be distinguished from other myopathic syndromes which warrant separate consideration by reason of their associated clinical features and certain therapeutic implications. Of prime importance among these are the endocrine myopathies: distinction from muscular dystrophy has already been considered.

Thyrotoxic myopathy, characterized by selective weakness of proximal muscles in either or both upper and lower limbs, may be associated with prominent muscular wasting. Other frequent features are loss of weight and at times a myasthenic form of fatigability which may show improvement with neostigmine (Millikan and Haines, 1953). Most cases occur in middle age and signs of thyrotoxicosis may be minimal even when clinical weakness is striking and the EMG indicates a myopathic (Gimlette, 1959). Thus, resemblance to polymyositis is obvious and since a raised

basal metabolic rate is frequent in both conditions, differentiation may be very difficult. Distinction depends, in essence, upon clinical evidence of thyrotoxicosis and the results of a radio-active iodine uptake test.

The muscular manifestations of hypothyroidism, characterised by enlargement of muscle together with slow contraction and relaxation, superficially resembling myotonia, should rarely be confused with polymyositis, although a case of the latter

teroid excretion and other appropriate tests will clearly differentiate this myopathy from polymyositis. A myopathy is also a feature of some cases of Addison's disease and occasionally of hypopituitarism (Zierler and Lilienthal, 1953) but clinical resemblance to polymyositis is unusual and the associated clinical and biochemical disturbances will serve to distinguish these conditions.

Prominent muscular weakness is frequent in hyperparathyroidism (Gutman et al., 1934). Such cases, and especially those described more recently by Vicale (1949) and Rowland (1958), which presented with weakness involving limb-girdle muscles, particularly in the legs may, by their rapidity of onset, resemble polymyositis. The absence of actual wasting of muscles and normal findings on electromyography and muscle biopsy help to exclude the latter, while radiographs of bones and estimations of calcium and phosphorus levels will indicate the presence of metabolic disease.

That polymyositis may be difficult to differentiate from myasthenia gravis is emphasized by the fact that long-standing cases of the latter disease may develop wasting and weakness of proximal limb muscles (Simpson, 1956). Furthermore, patients with polymyositis often show some fatigability which respond to neostigmine treatment. However, this is rarely so dramatic and so sustained as in genuine myasthenia. Serum enzyme estimations (Rowland and Ross, 1958) are of course normal in myasthenia, but so they are in most cases of subacute polymyositis and limb-girdle muscular dystrophy with which confusion is likely to arise. Muscle biopsy and intra-vital staining of the motor end-plate with methylene blue (Cöers and Desmedt, 1959) are often unhelpful so that the borderline between myasthenia gravis with muscular wasting and polymyositis with myasthenia remains ill-defined.

Sarcoidosis may closely resemble polymyositis, and though associated neurological findings are frequent (de Morsier et al., 1954) cases with muscular manifestations alone occur (Harvey, 1959). Muscle biopsy identifies this condition. Polyarteritis no-



Fig. 4

condition reported by Layani et al. (1955) did show myotonia.

Muscular wasting and weakness, common in Cushing's syndrome (Cope and Raker, 1955), although most often accompanied by other manifestations of the condition, may dominate the clinical picture (Montgomery and Welbourn, 1957; and Rowland, 1958). However, careful examination will usually reveal some evidence of moon face, hirsutes, hypertension and the like. If doubt remains estimation of the urinary ketos-

dosa, too, which rarely presents with widespread muscular pain and weakness (Radermeker and van Bogaert, 1952) is identified by the associated hypertension, albuminuria and peripheral nerve involvement (Daley and Miller, 1946).

Motor neurone disease and peroneal muscular atrophy which predominantly involve distal muscles will not as a rule be confused with polymyositis. When there is both proximal and distal muscular involvement electromyography will clearly distinguish the myopathic pattern of polymyositis from the neuropathic pattern of motor neurone disease, which rarely affects predominantly the proximal muscles. Chronic motor polyneuropathy, e.g. chronic anterior poliomyelitis or pseudomyopathic polyneuritis (van Bogaert and Radermeker, 1954) can also be distinguished by this means.

Group II Polymyositis with minimal skin changes or slight evidence of a "collagen" disease

These cases are grouped separately because at some time in the illness, signs of skin involvement or minimal evidence of some other "collagen" disease, is found. The skin changes may accompany or precede the onset of muscular weakness. Alternatively, dermal involvement may be present throughout illness but is very easily overlooked by the patients or their physicians.

Transient general malaise or slight fever, minimal joint pain and swelling, buccal ulceration, or periorbital and facial oedema may be present at some time in the illness. The Raynaud phenomenon may be observed, but the commonest sign is the presence of a slight erythematous rash, which often involves the face in butterfly distribution, but occasionally affects the limbs and trunk. The rash is usually moist and shiny, often of a violaceous hue, or it may be dry and scaly. An associated feature is that the skin of the hands, particularly at the base of the nails, may become unduly red, thin and tight, losing its elasticity. Ulceration of the skin sometimes occurs in exposed areas such as the heels, knuckles, elbows or hands, and cornified skin with extrusion of calcium in

similar distribution may also be observed. Slight changes in the joints closely resembling those of rheumatoid arthritis may be seen when dermal manifestations are absent. Infrequently there is generalised lymphadenopathy and splenomegaly. In cases of this group both the symptoms and signs of muscular involvement are so similar to those of subacute and chronic polymyositis as to make separate description unnecessary.

In the more acute cases, there is characteristic elevation of the sedimentation rate,



Fig. 5

and the serum aldolase and transaminase are often raised to values even higher than those found in early Duchenne type muscular dystrophy (Thomson et al., 1960); electromyographic and muscle biopsy findings are usually characteristic (Walton and Adams, 1958).

The course of the untreated disease is again subject to extreme variations. Rapid progression of muscular weakness is frequent at some stage of the illness, perhaps as part of a fluctuating course, and may be followed either by death, by arrest with

severe and permanent disability or by a spontaneous remission. Remission may be only partial but in three personal cases we have observed eventual complete recovery occurring without treatment after several years of gradual improvement. This course of events seems to be common in children but a prolonged and severely disabling disease may also occur in the young.

Group III Dermatomyositis: or severe "collagen" disease with associated muscular weakness

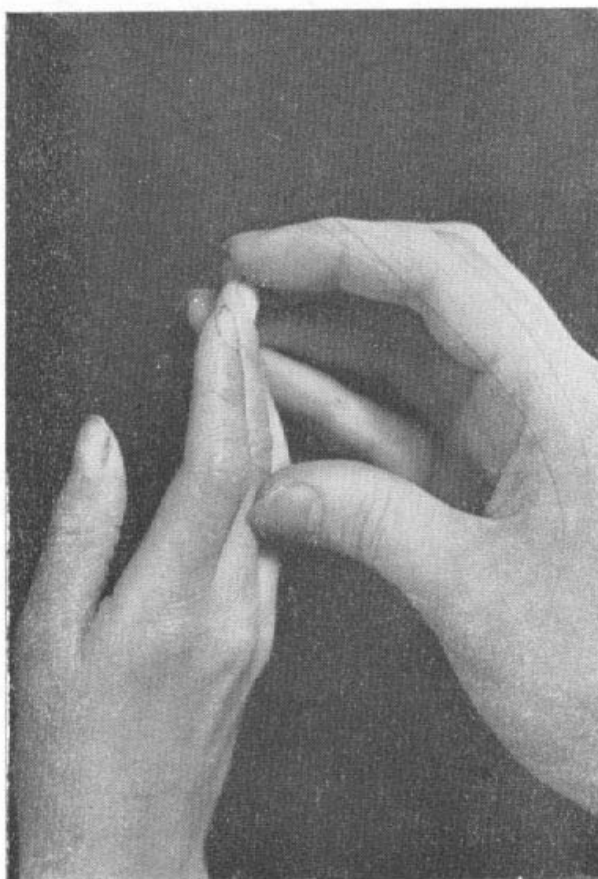
The symptomatology in these cases is dominated by the skin changes, though a proportion of cases manifest fever, malaise and weight loss, while a number also experience joint swellings, oedema of the face and limbs and/or mucosal ulceration.

The dermal manifestations are striking. A heliotropic erythematous eruption characteristically involves the face in butterfly distribution and extends on to the trunk and limbs. However, there is wide variation in the nature and severity of dermal manifestations. They may closely resemble lupus erythematosus, for the lesions may be photosensitive, and in addition to their butterfly distribution, they may have a raised, discoid character. In other cases dermal changes may call to mind seborrhoeic dermatitis, exfoliative dermatitis, lichen planus or poikiloderma, while in certain individuals, dermal manifestations, at first typical, gradually evolve into typical acrosclerosis or scleroderma (Figs. 4-6). In chronic cases, hypertrichosis, alopecia and diffuse cutaneous pigmentation may be seen. Subcutaneous haemorrhages in the hands and feet, and periungual oedema, characteristic of systemic lupus erythematosus, as well as of dermatomyositis, occur quite commonly. These changes have been extensively reviewed by Domzalski and Morgan (1955).

Oesophageal ulceration and haematemesis (Wedgwood et al., 1953) purpura, epistaxis and intestinal haemorrhage (Jager and Grossman, 1944) and intestinal ulceration (Karelitz and Welt, 1932; Texier, 1950) are other reported complications. Retinal changes in the form of macular and peripa-

illary floccular exudates and peripapillary haemorrhages associated with some papilloedema, may be seen, especially in more acute cases (Garcin et al., 1955; Delogu, 1959). Severe optic neuritis is rare — but Polster (1958) reports bilateral optic atrophy following a severe optic neuritis complicating dermatomyositis in a child.

Polymyositis also occurs as a complication of a variety of collagenoses, including rheumatoid arthritis, disseminated lupus erythematosus, and progressive systemic sclerosis. It is rare in polyarteritis nodosa,



Figs. 4-6. — A case of polymyositis with severe skin involvement, closely resembling the changes of acrosclerosis. In this case an acute polymyositic illness occurred with initial profound generalised muscular weakness, respiratory failure and a pericardial effusion. Spontaneous improvement was slow, but during the phase of recovery, skin changes and the hands and face, particularly, became prominent. This case has been reported previously by Walton and Adams (1958). Fig. 4, shows the facial appearance; Fig. 5, the skin changes and the hand; and Fig. 6, the slight flexion contracture of the fingers

in which disease polyneuropathy or infarction of several muscles sometimes occurs.

Where muscular involvement is not obvious, it may be possible to demonstrate that the degree of weakness is greater than any associated wasting. When the acute illness is over, a waddling gait, weakness of the shoulder girdle and neck muscles, possibly with pseudohypertrophy of the calves may, however, be present. Dysphagia due to involvement of the pharyngeal musculature and/or mucosa is common. Muscle tenderness is a feature of approximately a third of the cases and the muscles involved often feel tense and fibrotic.

Occasional accompanying features are signs of cardiac involvement (Garcin et al., 1955), confirmed by electrocardiographic findings; originally myocardial involvement was demonstrated by Oppenheim (1899). Pericarditis and pericardial effusion infrequently complicate the illness, and another rare complication, reported by Garcin et al. (1958) is auricular-ventricular dissociation with a Stokes-Adams syndrome.

Considerable variation in natural history is again evident, and accurate prognosis is extremely difficult in individual cases. The illness in the groups of cases is, however, more grave, and death is more frequent than in cases in Groups I and II. Thus, three of the eight cases described by Walton and Adams (1958) died of respiratory failure which was the result of the disease. A complete recovery from the untreated disease is rare and although a fluctuant course, slow, or rapid progression or even arrest may occur, severe residual disability is almost invariable. Gross contractures, widespread cutaneous ulceration, scarring and the presence of subcutaneous calcification may be added features. An extensive study of calcinosis in dermatomyositis has recently been reported (Muller et al., 1959). It appears that development of this complication can be expected in patients, especially children, who survive two or three years after the initial manifestations of the disease. Calcinosis, most frequently seen in the proximal limb musculature, although indicating poor functional recovery, appears to be a good prognostic sign with regard to survival.

Diagnosis in the group of cases depends upon the demonstration of muscular lesions in patients with florid skin change or a "collagenosis". Thus clinical evidence of muscular weakness and wasting, electromyographic and histological evidence of a myopathic lesion should be sought for confirmation of the diagnosis. When symptoms of proximal muscular weakness and wasting occur in a "collagenosis" during steroid therapy it should be recalled that these symptoms may arise as a result of treatment with any of these drugs and particularly with triamcinolone and dexamethasone, giving a clinical picture which resembles polymyositis (Perkoff et al., 1959). However, the clinical situation and fairly prompt recovery when therapy is discontinued or an alternative steroid is used, will confirm the diagnosis of steroid myopathy.

Group IV Polymyositis and dermatomyositis associated with malignant disease

These cases may closely resemble any of those already described, and are artificially separated on the grounds of their relation to malignant disease. Though muscular weakness may be the predominant symptom, clinical manifestations of a growth may be quite prominent; for instance, a history of cough, exertional dyspnoea and haemoptysis may lead to the discovery of a bronchogenic carcinoma. New growths of many different type and in many situations have been reported in association with polymyositis, but there is no clear temporal relationship between the two conditions. Evidence of the muscular disease may precede that of the neoplasm, sometimes by considerable periods. Alternatively, a neoplasm may be present long before polymyositis develops and the latter may remit though the neoplasm progresses and ultimately causes death. Again, removal of the growth, apparently completely, may or may not influence the muscle disorder. A common experience is that polymyositis shows an incomplete response to treatment and then relapses sufficiently severely to be fatal despite treatment, and the neoplasm is then discovered at autopsy.

Dermal and muscular manifestations closely resemble those described above in cases of the other three groups. Acute polymyositis with myoglobinuria is, however, unusual in association with new growth and indeed cases of the Group I type are somewhat less common in patients with cancer than those with florid skin manifestations. Probably the eight cases described by Henson et al. (1954) would be classified in our Group I but it is not yet certain whether carcinomatous myopathy is in fact the same as polymyositis; and many more cases of dermatomyositis with malignant disease have been reported, particularly in carcinoma of the lung. Rowland (1958) mentions that although dermatomyositis is relatively uncommon in patients with cancer, forty-one of 382 patients or 10.7% with dermatomyositis, in the combined figures of several reports, were shown to have this relationship. Rowland also lists 117 cases in the literature in which the tumour site was recorded. These were in descending order of frequency breast, stomach, lung, ovary, reticulo-endothelial system, uterus and vagina, unknown primary, gall-bladder, rectum, colon, kidney, prostate, sarcoma, oesophagus and pancreas. Isolated cases of myeloma, parotid, thyroid, pyriform sinus and laryngeal neoplasm are also recorded.

Treatment

Claims for the therapeutic efficacy of a wide variety of remedies are common in disease subject to spontaneous remissions. When, however, the number of remedies recommended in a disease is very large, it is usually apparent that no single treatment is uniformly successful. Among others, amino-acids, antibiotics, arsenic, calcium chloride, ephedrine, leucocyte suspensions, mepacrine, para-aminobenzoic acid, prostigmine, pyrotherapy, quinidine, quinine, salicylates, sulphonamides, testosterone, thyroid, vaccines, vitamin E and other vitamins and wheat germ have been used in polymyositis and dermatomyositis. None of these drugs have been shown to be effective in a convincing number of cases.

Polymyositis manifesting myasthenic fa-

tigability may be markedly improved by treatment with prostigmine or mestinon, but unfortunately many cases show only transient improvement and many others little or no response.

Unfortunately no controlled trials of ACTH or of cortisone and related drugs in polymyositis have been carried out, and present views on the efficacy of such preparations depend upon the experience of a number of writers who have treated relatively small numbers of patients. Thus, Everett and Curtis (1957) felt that while steroids appeared to have some beneficial effect, in dermatomyositis there was no real evidence that the basic course or outcome of the disease was altered, a view shared by Schuermann (1954) and by Carlisle and Good (1959) who referred particularly to children. In contrast Christianson et al. (1956) who expressed the opinion that steroid therapy was life-saving on occasions, have reported therapeutic responses in acute and chronic cases and even the disappearance of calcinosis. They claimed that even when malignant disease was present and progressing there may be a dramatic response to steroids. From these reports and from many isolated cases in the literature it has become apparent that patients with dermatomyositis generally show less response to steroids than do both adults and children with subacute and chronic polymyositis, in whom considerable improvement has been reported (Shy and McEachern, 1951; Eaton, 1954; van Bogaert et al., 1955; Walton and Adams, 1958). However, some similar patients with "pure" polymyositis show little or no response. It is apparent that cases in any of the subgroups described may prove refractory to steroid therapy but since there is no way at present of identifying such cases all should be given a trial of the treatment. Our recent experience with a total of fifty-two cases of all types, clearly indicates that the results are better the earlier in the course of the disease that the treatment is begun.

The usual regimen of treatment is to begin with 60 mgm. prednisone or prednisolone daily, reducing after four or five days to 40 mgm. daily and regulating main-

tenance therapy according to the response of the patient. We have found that in such cases it is sometimes necessary to persist with a very high dose of steroids (e.g. 50-60 mgm. prednisone a day) for several days or occasionally for weeks before a clinical response indicates that the dose can be reduced. Complications of steroid therapy such as haematemesis, psychosis, intestinal perforation, hypertension and diabetes, which must be borne in mind fortunately appear to be extremely rare in cases of polymyositis, in contrast to the usual experience in cases of rheumatoid arthritis. Treatment must be continued with the minimum dose of the drug which will keep the disease under control. The clinical response is the safest guide; and the treatment must be continued for from one to three years or even longer, before it can be withdrawn without clinical relapse. Although the value of the newer-protein anabolising steroids have not yet been assessed in polymyositis, when a clinical response is occurring in a case with considerable weight loss and wasting, the use of norandrostenalone or similar drugs together with a high protein diet may speed convalescence. The possibility of occult malignant disease must, of course,

always be borne in mind, as surgical removal of a tumour may lead to rapid improvement in the muscular disease. The importance of nursing and physiotherapeutic measures cannot be overemphasized. Great care may be necessary in the prevention of bed sores, especially in severely paralysed patients and those with marked skin involvement. In less severe cases active and passive movement and careful physiotherapeutic supervision will be necessary to prevent the development of contractures in the affected limbs and skeletal deformities and to aid the return of muscular power. Since prolonged bed rest may increase muscular weakness, early ambulation is indicated. Cases with severe respiratory weakness and associated pharyngeal involvement sometimes require intermittent positive pressure respiration while others may require treatment in a tank respirator. The development of urinary, respiratory and cutaneous infections may be expected, and should be treated early and vigorously with the appropriate antibiotic. Indeed in severe cases prophylactic antibiotics are needed in the first few weeks. Postural drainage may also be indicated in preventing or in treating respiratory infection.

SUMMARY

The clinical picture of polymyositis has been described. An arbitrary clinical classification of this syndrome, suggested originally by Walton and Adams (1958) has been adopted. The extreme pleomorphism of the condition has been stressed.

A review of some of the possible precipitating factors has been presented and mention has been made of the relationship of polymyositis to cancer.

The clinical features of the acute, subacute and chronic forms of the purely myopathic variety of polymyositis has been presented in some detail as it is these cases which present the greatest difficulty in recognition. The severity and rapidity of onset of the acute form has been stressed, together with the presence of myoglobinuria which distinguished the condition. In the

subacute and chronic cases, emphasis is laid upon the presence of weakness and to a lesser extent, wasting of proximal limb-girdle and neck muscles, and to the frequent complaint of dysphagia and of the Raynaud phenomenon. The various modes of progression in the untreated disease have been reviewed.

Problems of differential diagnosis are also reviewed and mention has been made of the various ancillary investigations which may be necessary to differentiate polymyositis from the other myopathies, and from certain neurogenic atrophies.

Features of polymyositis with minimal dermal changes or evidence of an associated "collagen" vascular disease have also been reviewed. The relative inconspicuousness of

dermal changes in such cases has been stressed.

Mention is also made of the features of polymyositis with more obvious skin changes (dermatomyositis) or complicating a clearly evident "collagen" disease, such as rheumatoid arthritis. Here diagnosis is easier, but certain difficulties which may arise have been mentioned.

In discussing the features of polymyositis associated with cancer, it has been indicated that dermatomyositis is the most commonly occurring variety of myopathy. The fact that there may be a considerable inter-

val between the onset of the myopathic process before the neoplasm is detectable, is emphasised.

The wide variety of remedies used in the disease have been briefly mentioned. The place of ACTH and cortisone has been reviewed and the opinion expressed that greatest benefit can be expected if these drugs are exhibited as early as possible in the disease. Also of paramount importance is skilled nursing care which together with physiotherapy can greatly influence the prognosis both with regard to survival and also the degree of residual disability.

RESUMEN

Se ha descrito el cuadro clínico de la polimiositis.

Se adoptó una clasificación clínica arbitraria de este síndrome, sugerida originalmente por Walton y Adams (1958). Se ha insistido en el extremo pleomorfismo de la afección.

Se pasó revista a algunos de los factores precipitantes y se mencionó la relación de la polimiositis con el cáncer.

Se presentó con cierto detalle el cuadro clínico de las formas agudas, subagudas y crónicas de la variedad puramente miopática de la polimiositis, porque se piensa que son estos casos los que presentan la mayor dificultad para su reconocimiento. Se subrayó la severidad y rapidez del comienzo de la forma aguda, junto con la presencia de mioglobulinuria, lo cual distingue la afección. En los casos subagudos y crónicos, se insistió en la presencia de debilidad y en menor grado de atrofia de los músculos proximales de los miembros y del cuello a la frecuente queja de disfagia y del fenómeno de Raynaud. Se señaló las distintas modalidades de evolución en la enfermedad no tratada.

Se revisaron problemas de diagnóstico diferencial y se mencionaron las distintas investigaciones auxiliares que pueden ser necesarias para diferenciar la polimiositis de otras miopatías y de ciertas atrofias neurogénicas.

También fueron considerados cuadros de polimiositis con cambios dérmicos mínimos o evidencia de una enfermedad vascular del colágeno asociada.

Se subrayó la relativa poca importancia de los cambios dérmicos en tales casos.

Fueron mencionados cuadros de polimiositis con cambios de la piel más evidentes (dermatomiositis) o complicando una enfermedad del colágeno evidentemente clara, tal como la artritis reumatoidea. Aquí el diagnóstico es más fácil; pero se citaron algunas dificultades que pueden aparecer.

Al discutir los cuadros de polimiositis asociados con cáncer, se indica que la dermatomiositis es la variedad de miopatía que ocurre más a menudo.

Se insistió en el hecho de que puede haber un intervalo considerable entre el comienzo del proceso miopático y el momento en que el cáncer es detectable.

Se mencionó brevemente la gran variedad de remedios usados en esta enfermedad. Se consideró el lugar del ACTH y Cortisona y la opinión expresaba que el mayor beneficio puede esperarse si estas drogas son usadas precozmente en la enfermedad. Es también de importancia fundamental un cuidado de enfermería experimentado, el cual junto con la fisioterapia puede influir grandemente en el pronóstico, tanto en lo que se refiere a la sobrevivencia, como al grado de la incapacidad residual.

RESUME

On a décrit le tableau clinique de la polymyosite. On a adopté une classification clinique arbitraire de ce syndrome, suggérée originalement par Walton et Adams (1958). On a insisté dans l'extrême pléomorphisme de la maladie.

On a passé en revue quelques uns des facteurs précipitants on a mentionné la relation de la polymyosite avec le cancer.

On a présenté avec certain détail le tableau clinique des formes aiguës suraigües et chroniques de la variété purement myopathique de la polymyosite parce que l'on pense que ce sont ces cas, ceux qui présentent la plus grande difficulté pour les reconnaître, on a souligné la sévérité et la rapidité du commencement de la forme aiguë, avec la présence de myoglobulinurie ce qui différencie la maladie. Dans les cas suraigus et chroniques on a insisté dans la présence de faiblesse et en moindre degré d'atrophie des muscles proximales des membres et du cou, à la fréquence plainte de dysphagie et du phénomène de Raynaud.

On a signalé les différentes modalités d'évolution dans la maladie non traitée.

On a étudié des problèmes de diagnostic différentiel, et on a mentionné les différentes investigations auxiliaires que peuvent être nécessaires pour différencier la polymyosite de d'autres myopathies et de certaines atrophies neurogéniques.

On a considéré aussi des cas de polymyosites avec des changements dermiques mi-

nimes ou l'évidence d'une maladie vasculaire du collagen associé.

On a souligné le peu d'importance relative, des changements dermiques dans ces cas.

On a mentionné des cas de polymyosites avec le changement de la peau les plus évidents (dermatomyosite) ou compliquant une maladie du collagen évidemment claire, tel comme l'artrite rhumatoïde.

Ici le diagnostic est plus facile; mais on a cité quelques difficultés qui peuvent apparaître.

En discutant les cas de polymyosites associés avec des cancers on indique que la dermatomyosite est la variété de myopathie qui arrive le plus souvent.

On a insisté sur le fait qu'il peut y avoir un intervalle considérable entre le commencement du développement myopathique et le moment où le cancer est détectable.

On a mentionné brièvement la grande variété de remèdes employés dans cette maladie. On a considéré la place de l'ACTH et de la cortisone et l'opinion exprimée que l'on peut attendre le plus grand bénéfice si ces drogues sont employées précocement dans la maladie. C'est aussi fondamental un soin d'infirmier expérimenté, lequel associé avec la physiothérapie peut influencer amplement dans le pronostic autant dans ce qui concerne la survie qu'au degré de l'incapacité qui reste.

ZUSAMMENFASSUNG

Die Autoren beschreiben das klinische Bild der Polymyositis, wobei sie die willkürliche klinische Klassifizierung, die ursprünglich von Walton und Adams (1958) vorgeschlagen worden ist, angewandt haben. Sie betonen den ausserordentlichen Pleomorphismus dieser Krankheit.

Es werden einige mögliche auslösende Faktoren sowie auch die Beziehungen

zwischen der Polymyositis und dem Krebs erwähnt. Es wird das klinische Bild der akuten, subakuten und chronischen Form der rein myopathischen Spielart der Polymyositis etwas detailliert dargestellt, in der Annahme, dass es gerade diese Fälle sind, welche die grössten Schwierigkeiten für die Diagnose bieten.

Die Schwere und die Schnelligkeit des Beginns der akuten Form, als auch das

Auftreten der Myoglobinaemie, die diese Form charakterisiert, sind hervorgehoben worden. In densubakuten und chronischen Faellen werden die Koerperschwaeche und, in geringerem Grade, die Atrophie der proximalen Extremitaetenmuskeln und der Halsmuskeln wie auch die haeufigen Klagen ueber Dysphagie und das Raynaud'sche Phaenomen betont. Es wird ueber die verschiedenen Arten des Vorschreitens der unbehandelten Faelle gesprochen. Dann hebt man die Probleme der Differentialdiagnose hervor sowie auch die verschiedenen. Hilfs- Untersuchungen, welche notwendig sein koennten, um die Polymyositis von anderen Myopathien und gewissen neurogenen Atrophien zu untrescheiden.

Es sind auch Formen von Polymyositis mit minimalen Hautlaesionen oder Merk-

malen einer beigeordneten kollagenen Gefaesserkrankung besprochen worden.

Und es ist die Aufmerksamkeit auf die relative Unbedenklichkeit der Hautveraenderungen in diesen Faellen gelenkt worden.

Die grosse Anzahl von Medikamenten, die bei dieser Krankheit angewandt werden sind kurz erwaeht worden. Die Bedeutung von ACTH und Cortison ist besprochen worden, wobei die Meinung vertreten wurde, dass man den groessten Nutzen erwarten kann, wenn die Medikamente so fruehzeitig wie moeglich bei der Krankheit angewandt werden. Es ist auch von groesster Wichtigkeit, die erfahrene Pflege, welche zusammen mit der Physiotherapie enorm die Prognose beeinflussen kann, sowohl hinsichtlich der Ueberlebenserwartung als auch des Grades der zurueckbleibenden Invaliditaet.

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Metabolic Factors in the Muscular Electrogenesis

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INTRODUCTION

The present paper deals with the E.M.G. patterns occurring in any dysmetabolic muscle diseases (professional poisonings, occlusive arterial diseases of lower limbs) and the E.M.G. changes observed with various biological treatments of any pathological muscle conditions.

The muscle tissue may be considered as a complex entity, with a very extensive physiological importance provided by numerous factors for a constant interaction between central and peripheral mechanisms.

The modern knowledge of the metabolic activities of muscle fibers allows us to consider from a pathogenetic dynamic (dysmetabolic) point of view the neuromuscular disorders. We may remember the EMG findings in toxic myopathies or chronic obstructive arterial diseases in which the muscle fiber or the lower motor neurone itself appear to be affected.

We will discuss in the following pages both the biochemical and the EMG aspects of various professional intoxications (e.g., carbon monoxide, carbodisulphide and lead poisonings) and the biochemical and EMG findings of arterial diseases.

PERSONAL RESULTS

In carbon monoxide poisoning a very frequent damage of muscle fibers can be observed, with changes in fundamental parameters of action potentials (duration and amplitude of single spikes). Such

findings are transitory and confirm the experimental results by Lorente De No', Shanes and Hopkins, Fenn and Gershamm upon the changes in membrane potential from acute anoxia.

Systemic explorations by various muscle groups (bic. brachii, flex. radial. carpi, adductores, gastrocnemii) of twenty patients suffering from chronic carbon disulphide poisoning have shown normal or borderline findings in seven subjects, a clearcut "neurogenic" pattern in 5 cases, "myogenic" tracings in another 5 and findings of mixed type in the others. These results confirm the frequent involvement of neuromuscular system by carbon disulphide poisoning and show the hypothesis of a mixed pathogenesis to be very probable. The vascular lesions occurring by carbon disulphide poisoning may be probably responsible either for the EEG or for the EMG patterns.

In lead intoxication very frequently were observed by Serra and colls. in 23 workers "neurogenic" tracings, as was previously observed by Marinacci and Thiebaut & colls. Santanelli and Serra have described from a clinical and EMG point of view in a whole family poisoned with lead arseniate the constant clinical and EMG involvement of extensor muscles. EMG and clinical patterns similar to lateral amyotrophic sclerosis were described by Guardascione and colls. in a patient with clinical and biological findings of lead intoxication. Comparative EEG, EKG and EMG investigations by Sessa and Serra in patients affected with lead myocardic and

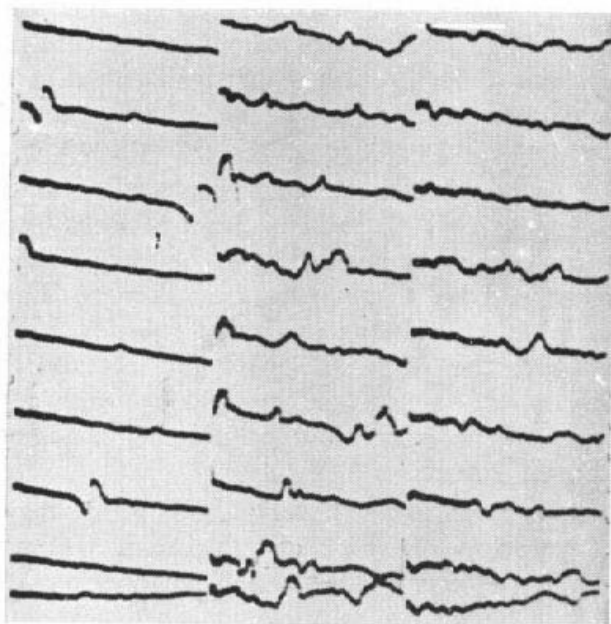


Fig. 1. — Action potentials of MM. bicipites brachii in acute carbon monoxide poisoning

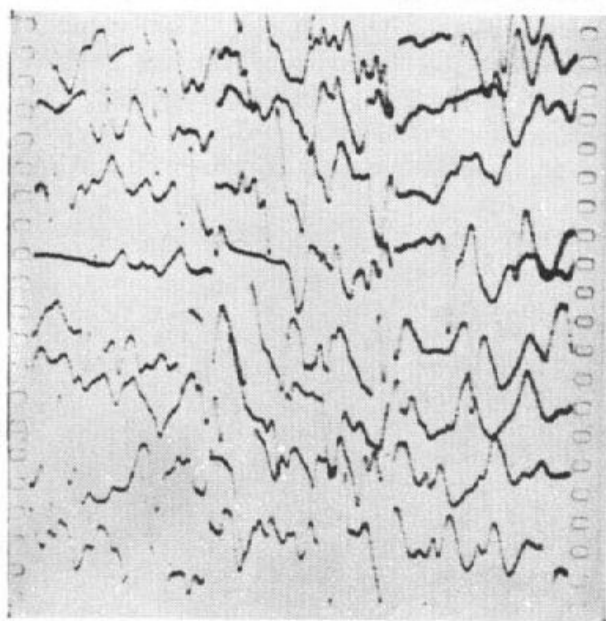


Fig. 2. — Same muscles after administration of Cythochrome

coronary diseases have shown the very significant concordance between the EEG, EKG and EMG findings, for which probably may be responsible the vascular lesions and the involvement both of centres and nerve fibers produced by lead.

The ischaemic genesis by this intoxication was confirmed by the bioenzymatic action of lead upon oxydoreductive ferments.

Studying the EMG patterns of occlusive arterial diseases the concept was introduced to account for the behavior of recruitment of motor neurones in chronic ischaemic conditions. Patients with chronic obstructive arteriosclerosis often show definite EMG changes. These findings are demonstrative of vascular insufficiency and can be correlated with the clinico-pathological data: a significant correlation between types of EMG abnormality and both trophic and vegetative troubles of the skin was frequently observed. In chronic tissue ischaemia produced by obstructive arterial disease Serra and cols. have frequently observed a very important reduction of muscle action potentials, as it may be observed in acute anoxia from carbon monoxide poisoning. This innervation deficiency could be enhanced, in arterial diseases of more severe grade, or detected in slight arteriopathic conditions by means of smoking test. Using this probe the efficiency of regulating vasomotor mechanism could be revealed, with informations of good prognostic preoperative value.

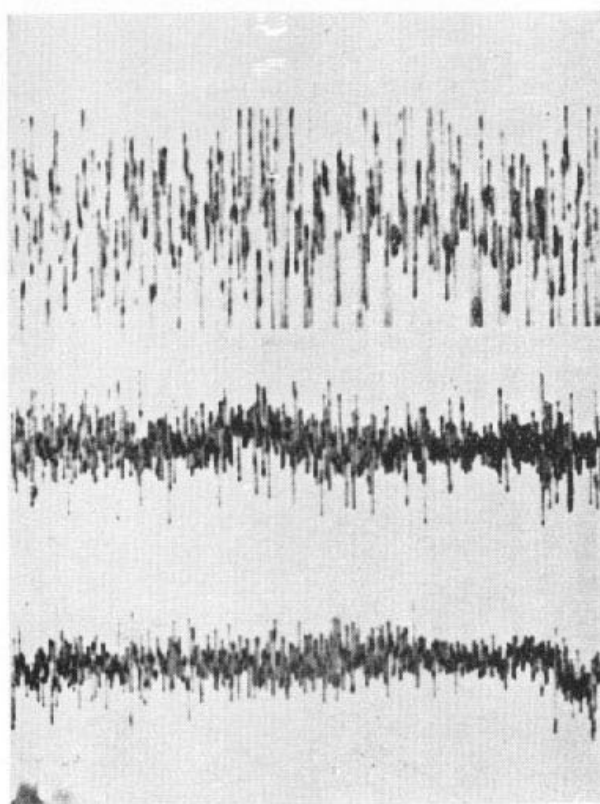


Fig. 3. — EMG of flexores radiales carpi in chronic carbon disulphide poisoning

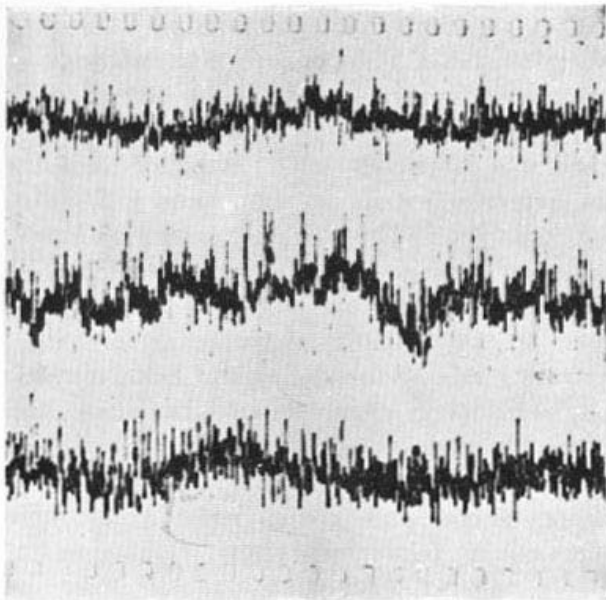


Fig. 4. — EMG pattern of gastrocnemii in lead chronic intoxication

The influence of both enzymic and metabolic factors upon electrical muscle activity was also investigated. We have recorded a good improvement of action potentials recruitment during voluntary

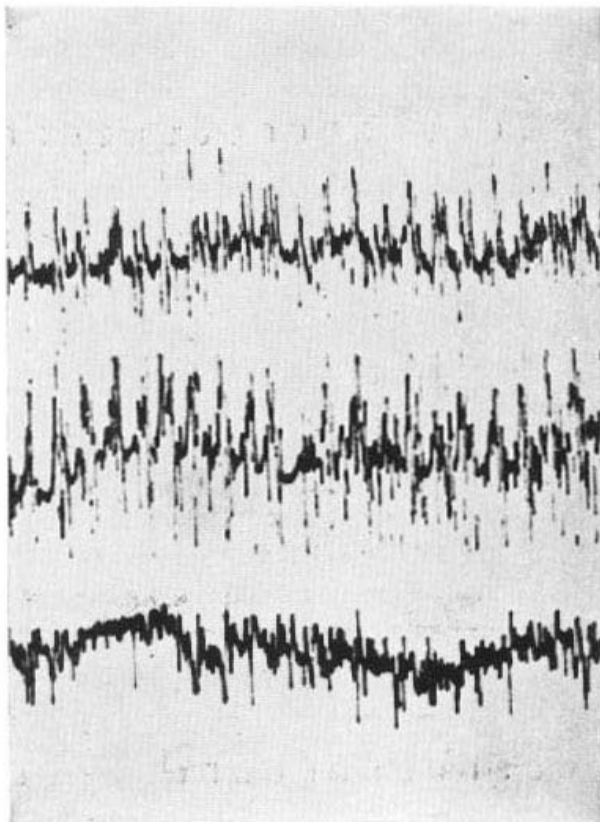


Fig. 5. — EMG record of tricipites brachii after acute familiar intoxication by lead arseniate

activity after intravenous administration either of cythochrome or of glucosa solution. In these experimental conditions the decrease of mean rate of activation of the muscle fibers as fatigue develops could be avoided.

A comparison between the records before and after this treatment demonstrates the source of action potentials to be very likely influenced by these metabolic factors. The available knowledge as to the relationships between the blood supply, the metabolic activity of a muscular district and its electrical activity may explain the above exposed results.

In ten volunteers who had temporary interruption of their circulation a similar E.M.G. pattern was recorded which may be influenced by the administration of various enzymic substances.

In arterial occlusive diseases the EMG investigations are thus able to give definite objective findings as well as the degree and the locations of the lesions. The value of EMG recording for differentiating genuine vascular diseases from malingering and hysteria is obvious.

As it is well known, in the ischaemised

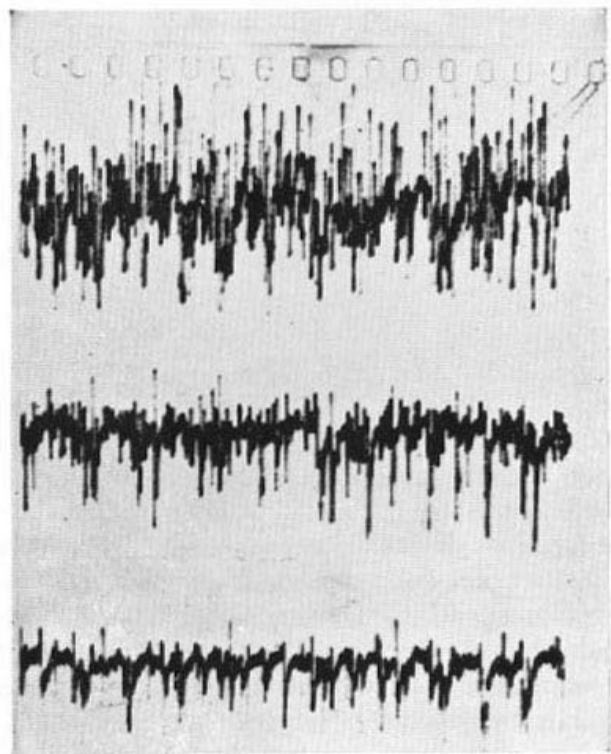


Fig. 6. — Innervation patterns of gastrocnemii arteriopathic, stage II of Fontaine

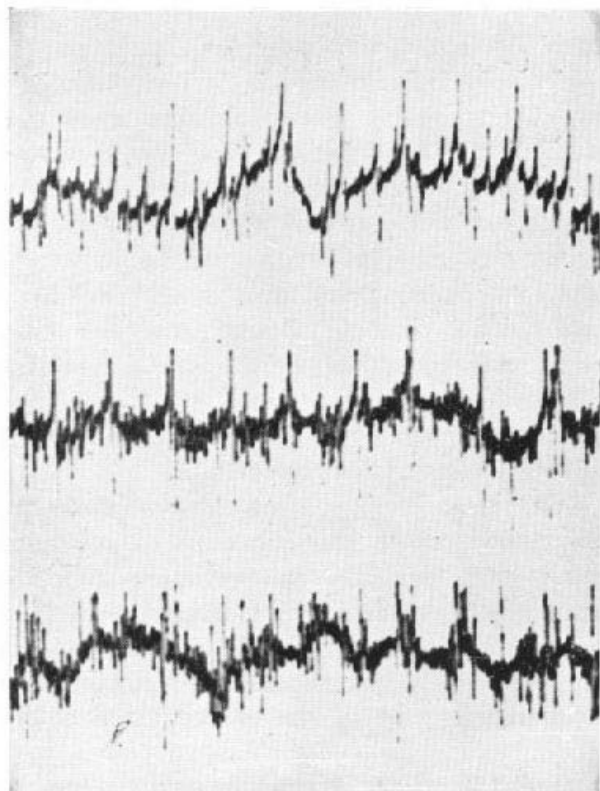


Fig. 7 a) — Chronic obstructive arterial disease, stage III of Fontaine gastrocnemii muscles

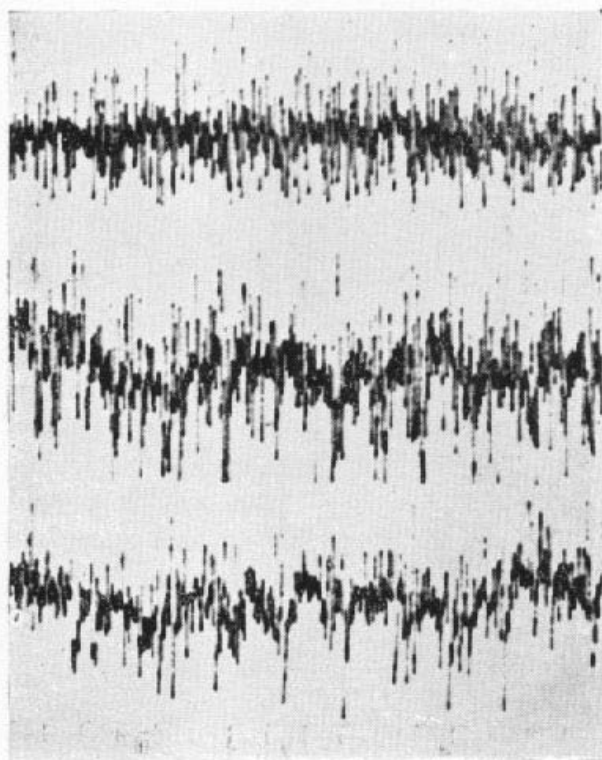


Fig. 7 b) Same muscles after surgical treatment (lumbar sympathectomy)

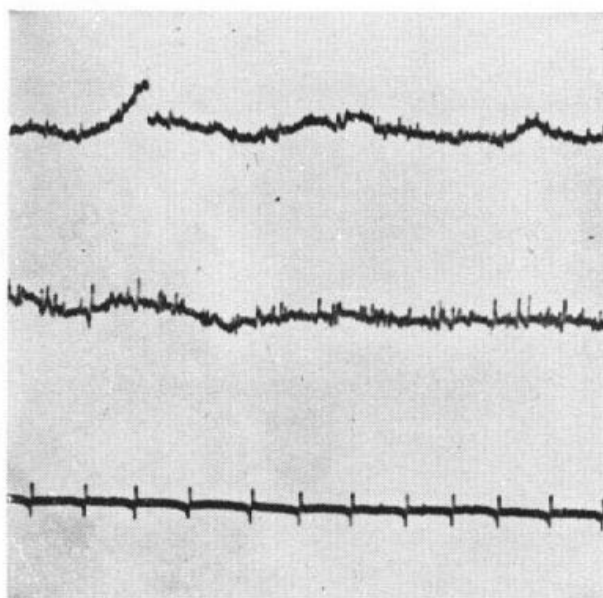


Fig. 8. — Chronic obstructive arterial disease of lower limbs, IV stage of Fontaine: gastrocnemii muscles

muscle we find very important troubles in iron metabolism with involvement of respiratory enzymatic chains.

The correction of oxydoreductive deficiency of ischaemised muscle can be demonstrated by the EMG changes during and after administration of various metabolic substances. Thus we have tried to correct the deficit of muscle glycogene and the related troubles of action potentials by giving to ischemic tissues various high-energy rich substances or by administering into the muscle circulation iron solutions. After this treatment we have observed a very important activation of muscle electrogenesis either in basal conditions or under ischaemic or fatigue conditions in volunteers.

The muscle action potentials innervation resulted to be improved also after administration of DPN, cocarboxylase and other enzymes of respiratory chains (riboflavin-phosphate, piridoxine) and ascorbic acid. With intraarterial administration of ascorbic acid the muscle activity both under normal or ischaemic and fatigue conditions could very well be improved with a clear-cut influence of this vitaminic substance upon the parameters of muscle action potentials.

As it is known, in normal conditions too,

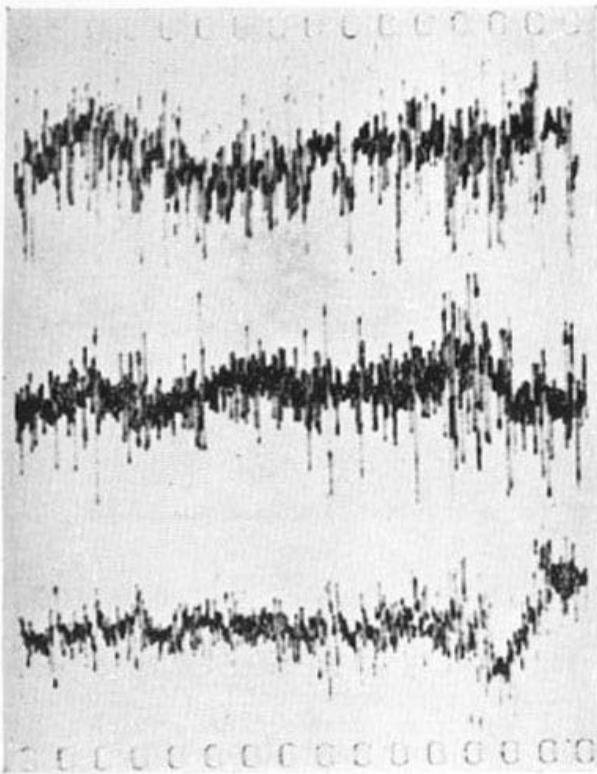


Fig. 9 a) — Innervation pattern from bicipites brachii of normal, during prolonged fatigue

muscle fatigue does not depend on the disappearance of glycogen and on the accumulation of lactic acid but on the disappearance of ATP (adenosine triphosphate) and other high energy phosphated compounds (Aubert).

This explains how in other conditions of pathological fatigue ATP can prevent the phenomena of fatigue (Albeaux-Ferner Bougard and Romani).

Bearing in mind the very important changes in ATP content in the ischaemic muscle or in the neurogenic conditions I have also tried to investigate the influence of such high-energy rich substance upon the muscle electrogenesis.

Under normal conditions ATP itself can increase the electrical muscle activity whilst the increase is more notable if conditions of innervation deficiency, or fatigue, are previously induced in the muscle.

The assumption that not all motor units have been lost in acute anterior poliomyelitis and that is therefore necessary to revive these still vital motor units as soon as possible has led us to try a new biological

method. The studies were performed on a series of over 300 patients with paretic sequelae of various muscles from poliomyelitis. Comparative investigations were performed in 10 patients with polio-palsies and other 12 patients with neurogenic conditions of different type, both from the paretic muscles and from the healthy contralateral ones, prior and after the infiltration into muscle fibers, just near the motor end plates of a solution containing the fundamental metabolites of the contraction (myosin, ATP, sodium and potassium) in optimal proportions.

According to Jusevitch observation that restoration of muscle function in acute anterior poliomyelitis as well as in other neurogenic conditions is accompanied by the normalization of the bioelectric processes, our study has represented an attempt of quantification of the effects of this bio-

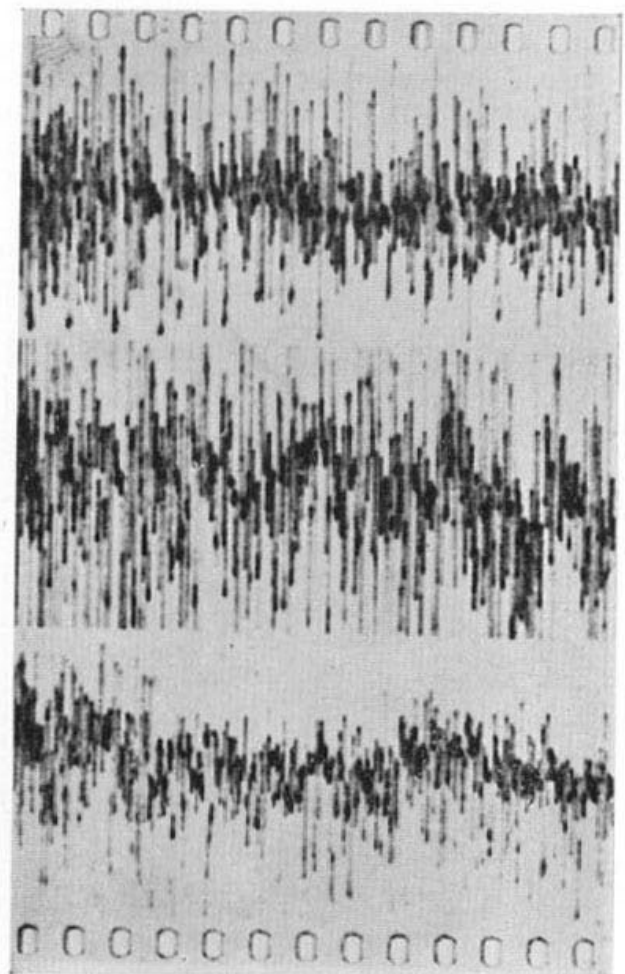


Fig. 9 b) — Same muscles, during fatigue, after administration of ascorbic acid

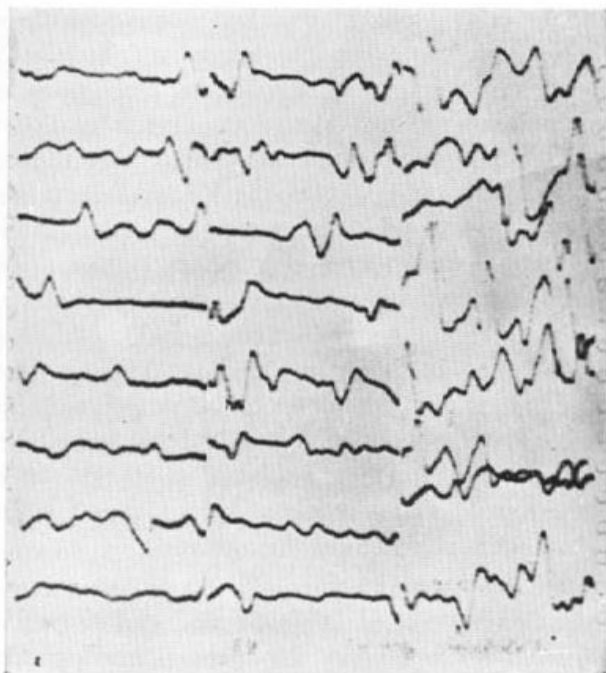


Fig. 10 a) Action potential of normal muscles (bic; brachii) after prolonged ischaemia

logical treatment, by recording the changes in muscle action potentials during and after the therapeutical treatment. The results observed consisted in increasing of action

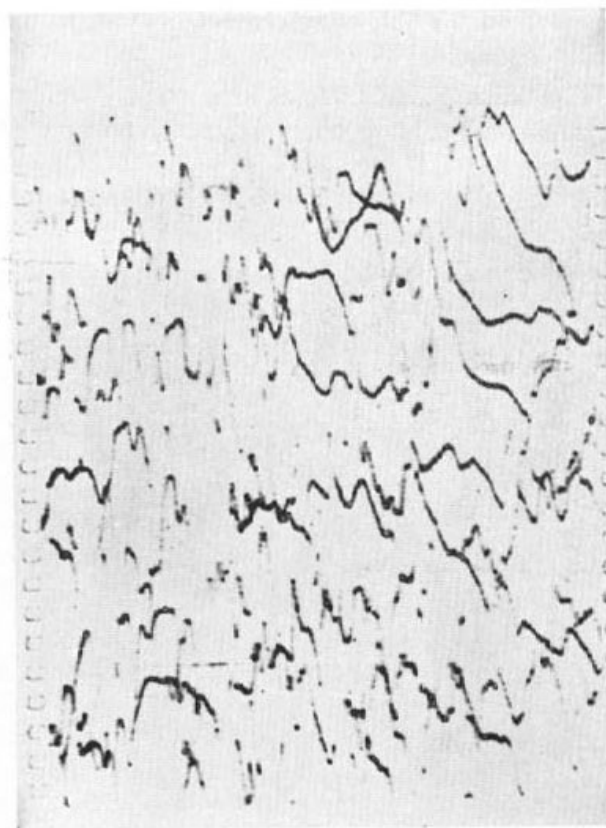


Fig. 10 b) — Same muscles after administration of cythochrome

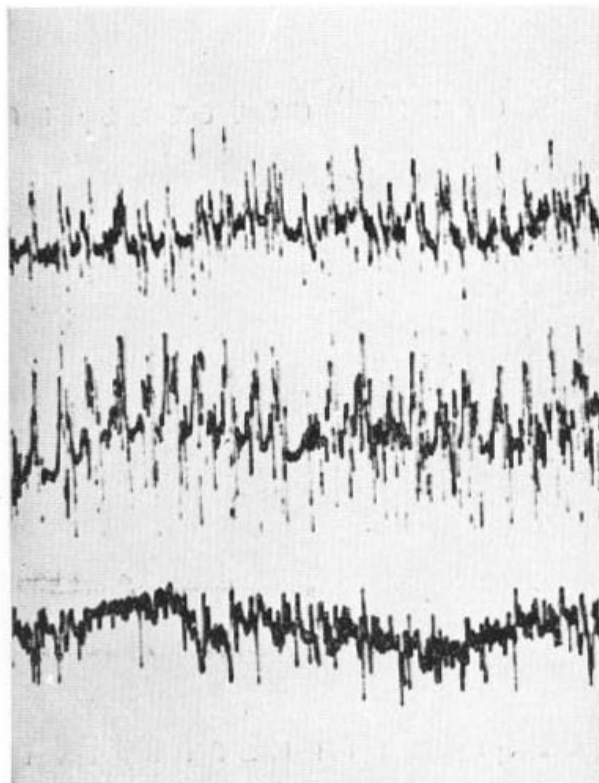


Fig. 11 a) — Innervation pattern of normal muscles (bic brachii) after prolonged simultaneous fatigue and ischaemia

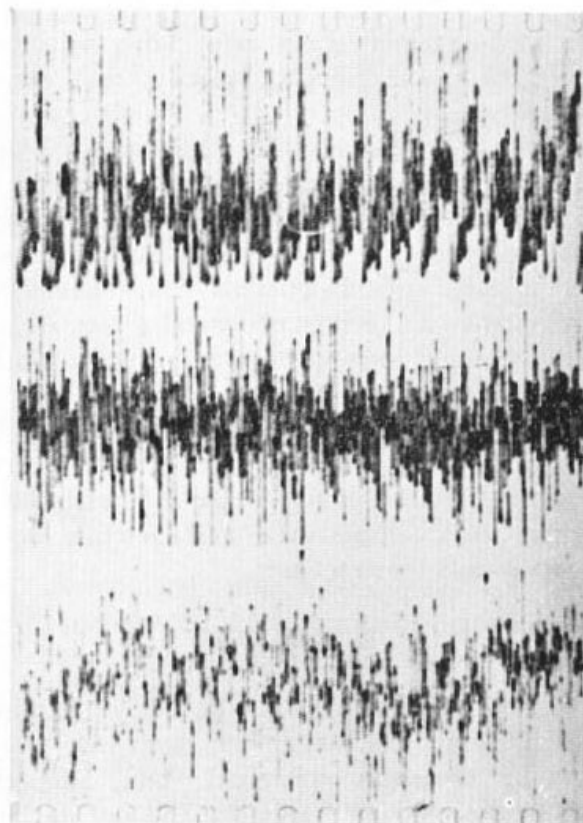


Fig. 11 b) — Quick recovery of innervation pattern from the same muscles after administration of ATP

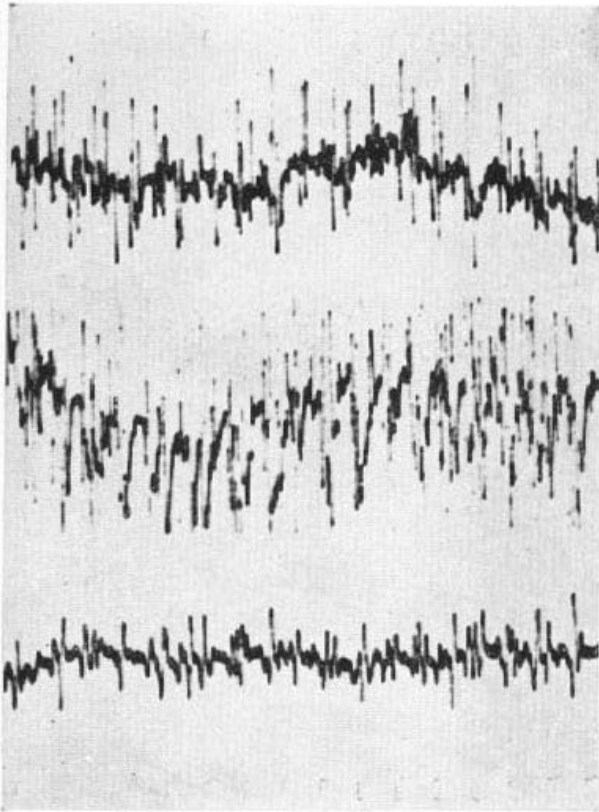


Fig. 12 a) — Reduction of innervation pattern of quadriceps m. in case of neuropathy

potentials innervation rate, with improvement of parameters of motor unit action potentials.

Further more we have tried to influence both innervation rate and the parameters of single motor unit potentials by the administration of high-energy phosphate bounds. By means of Buchthals' multielectrode technique we have observed a significant variation in motor unit territory induced by the above exposed energizing substances. The addition to muscle circulation of ATP solutions leads very probably to the activation of still inactive muscle fibers, modifying their impedance and setting up a propagated contraction.

DISCUSSION

The interpretation of the above exposed results may be based on both the well-known neurophysiological data and the recent discoveries regarding the normal and pathological biochemistry of the muscle.

As it is well known every muscle receives innervation from various motor units

which may even overlap one another within the same muscle segment (Fulton). So it happens that while in one muscle fasciculus we find complete muscular atrophy, in another one the fibres are intact and healthy. (G. Wolfart). Recording from various points of the same paralysed muscle one can obtain the graphic pattern of these histopathological data on the electromyographical record (Buchthal). Hodes (1948) has succeeded in demonstrating that the first motor units to be affected by the polio-virus are those whose fibres have the highest conduction speed (70-80 m. per sec.); while those with a lower speed (30-40 m. per sec.) may be spared.

The most recent data on the gamma control of movements (Granit and colleagues) allow us to presume the presence of more refined regulating mechanisms which we shall examine after having reviewed the biochemical data.

As it is well known, in a muscle affected by a neurogenous lesion, complex bio-humoral changes are to be found, of which we list the most important, referring to the monograph by Scalabrino and Bianchi for details, and to a recent electromyographic study by us.

The kalium in muscles affected by neurogenous lesion is greatly reduced compared

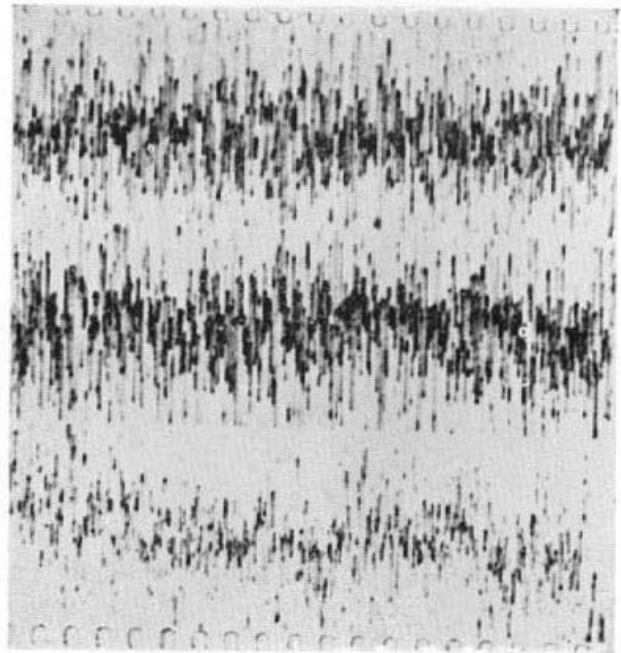


Fig. 12 b) — Same muscles after administration of ATP

to normal values (Dreyfus and Schapira), such a reduction being clearly proportional to the anatomic damage (Leulier and colleagues; Cicardo and Gurevitch, Scalabrino and Bianchi, Buchthal).

The sodium undergoes variations in the opposite sense, so it is easy to find pathological percentages of sodium greater (160 mgr.%) than the normal ones established by the material of Iseri, Alexander, Mac Caughern, Boyle, Myers and Pratt.

Muscle adenosinetriphosphate content diminishes sharply, even to the point of disappearing if the pathological conditions persist for a long time. (Green, Mac Farlane).

In the denervated muscle, a considerable disturbance of Krebs metabolic cycle is to be found, as is demonstrated by the increased pyruvic acid content and the decrease in the citric acid content (Morgano and Abbona).

Chemical fractionation and electrophoretic examination give us important information on the behaviour of muscle proteins; so we know today that Szent-Györgyi's myosin A myosin p.d.) decreases with a simultaneous decrease in ATP-ase activity, associated with myosin (Michelazzi, Mor, Dianzani). In the muscle affected by acute anterior poliomyelitis, the electrophoretic reveals:

- a) reduction of the myosin and myogens
- b) increase in the myo-albumin curve
- c) decrease in the $\frac{\text{myosin}}{\text{myogen}}$ relation

(Ghigliotti and La Medica).

Many factors (reduction of ATP, modification in ionic balance), cause a reduced yield of the contractile proteins. Furthermore, the decreased ATP content in the denervated muscle causes an acceleration in formation of acto-myosin.

Through the complex changes in the glycogenmyosin potassium molecular aggregate, the potassium ion moves freely across the membrane into the extra cellular space.

The increase in sodium content depends on the insufficient energy processes regulating the sodium pump (as Eccles has brilliantly demonstrated).

The fall in the demarcation potential of

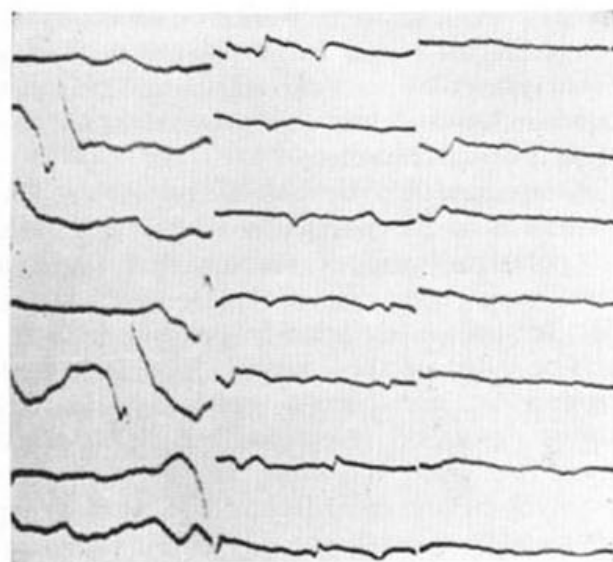


Fig. 13 a) — Action potentials of "polio" muscles (cuadricipites)

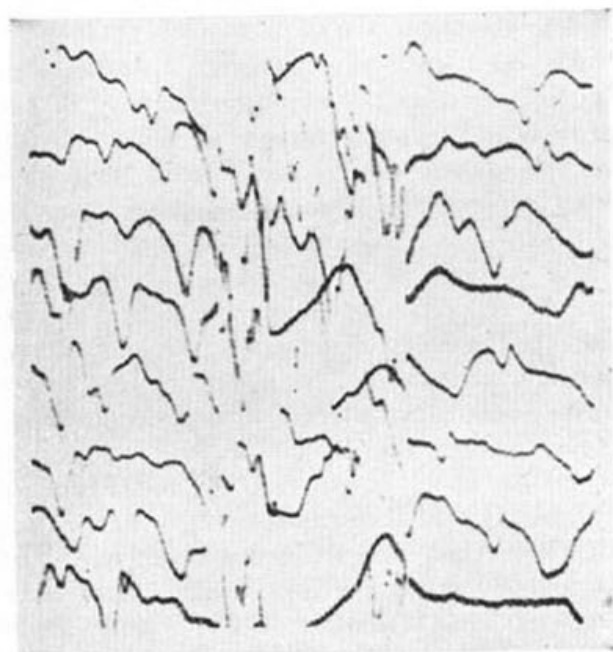


Fig. 13 b) — Same muscles after repeated administration of ATP

the denervated muscle depends on the above-mentioned biochemical, metabolic, physical changes occurring in the muscle after denervation:

- a) the low glycogen, ATP, phosphocreatine contents
- b) the diminished succinic-dehydrogenase and cytochrome-oxidase activity. No apparent correlation between succinic-dehydrogenase activity and cytochrome-oxidase activity in the muscle could be histoche-

mically evidenced (Beckett and Bourne).

Muscles taken from persons suffering from muscular as neuromuscular disorders contain less succinic-dehydrogenase activity than normal muscle.

Consequently the necessary energy to maintain those particular ionic gradients of potassium and of sodium that regulate the membrane potential (Bensett, Ware, Mc Intyre) is deficiently produced.

The value of these factors in muscle electrogenesis has been emphasized in our above described researches which demonstrate that even the most pathological electromyographic records undergo very sharp changes (improvement in the innervation regime, increase in the amplitude and duration of the single motor unit potentials), when the addition of high energy phosphate bounds or respiratory enzymes to the muscular tissue is made available.

As concerns the results obtained in "polio" muscles the explanation may be the provisional interpretation as follows: not all the motor units have been lost in a muscle territory affected by acute anterior poliomyelitis: this is proved both by the EMG records prior to biological treatment and by the changes in muscle action potentials parameters observed after our therapeutical treatments. Many surviving motor units probably undergo a compensatory increase, under the effect of the biological stimulus as it is proved by recording of potentials of abnormally high amplitude and abnormal length, quite often found in intreated poliomyelitic cases (Lefebure, Bernard and Lecouer; Pinelli and Buchthal) which are the rule after the biological treatment we carried out.

We may therefore assume that the employment of a solution consisting mainly in electrolytes, ATP and myosin, on the concerted action of which the muscular contraction and decontraction depend (compare the data of Huxley and Szent-Györgyi) may stimulate the fibres of the motor units inactive but not irremediably affected by polio-virus. The mechanism by which stimulus is carried out may not be quite so direct.

Each of the ingredients of the liquid we used is definitely active in itself: the ka-

lium, the ATP and the sodium are efficacious in themselves, but the high activity of the method probably depends on their synergistic pharmacological action.

This activation is either directly set up on the periphery, due to a direct substitutive phenomenon, or a more complex intervention of alpha impulses and responses must be supposed.

It is of considerable importance that the excitability of motoneurons does not disappear at the same moment in all motor units, a stimulation limit remains which may be a little higher, being conditioned by the anatomo-functional state of the reticular substance which, as it is well known, always undergoes more or less extensive damage in cases of polio. (O'Leary, King and Meagher).

In any case it is clear that the electromyographic alterations which we have noticed, tending to persist even after the therapy is over, demonstrate a basic concept in clinical electromyography, suggested by Buchthal, namely that the variations in muscle action potentials are more important than the alteration in the number of active fibres of each motor unit. Lastly it is clear that the above mentioned variations may be induced by the addition of high energy phosphate bounds.

If we keep in mind the recent experimental data obtained by Eccles and colleagues we realise that only at the cellular level is it possible to specify the origin of the complex electrochemical phenomena of living tissues and of the variations in potentials which we noted.

The above exposed results suggest and confirm a recent definition by Mc Eachern that the lower motor neurone is one of the most specialized structures in the body, which must be considered not only in terms of static histology, but in terms of biochemistry. A stream of liquid nutrients constantly flows from the nerve cell, a true "biochemical factory", to reactive peripheral structures".

In the light of recent discoveries in enzymology, several theories on muscle histopathology should be revised: thus not only deficiencies but also conditions of enzymatic disequilibrium (for example func-

nal alterations between oxidating cozymase (DPN) and oxidizing enzymes, in which the co-enzyme is not required (succinic-dehydrogenase) should be considered as pathological factors capable of altering cellular activity. The influence that deficiencies and enzymatic destruction have on cellular activity, throws considerable light on the physiotherapy and the clinical aspects of acute anterior poliomyelitis, in which, as in other neuropathological fields, a sharp demarcation cannot be observed between functional pathology and structural pathology. "Cellular structures — as Ciaranfi notes — closely depend on the biochemical and enzymatic cell activity".

The E.M.G. studies on neuromuscular transmission lead us to emphasize the strong correlation existing either between morphological and functional properties or between "biochemical periphery" and muscle electrical activity. As Buller and cow. have

shown, the neural influence on muscle speed is not exerted by nerve impulses as such. Tower, Eccles, Luco and Eyzaguirre have emphasized the possible relationship of this neural influence on muscle contraction to the "trophic" influence, presumably distinct from the postulated fast and slow influences on the contractile mechanism of the muscle (Buller & cow.).

Both peripheral and central mechanisms can surely cooperate to same extent in normal muscles and probably in many dysmetabolic conditions that lead to fatigue and, in the extreme cases, to the myopathic states.

The same gamma control of movement, the electrical activity of mammalian intrafusal fibres and the motor regulation of spindle discharges appear very likely to be influenced and conditioned by these local metabolic factors.

SUMMARY

AA. review their personal findings from various EMG approaches to dysmetabolic myopathies, especially to the toxic professional diseases and occlusive arterial diseases of lower limbs.

The EMG patterns observed by the various professional poisonings, (changes in muscle action potentials by acute carbon monoxide poisoning, reversible with return of oxygen supply or after administration of respiratory enzymes; tracings of mixed type, *neurogenic* or *myogenic*, by carbon disulphide poisoning; *neurogenic* patterns by lead poisoning) allow to include these morbid states among the toxic dysmetabolic involvement of muscle fibers.

In chronic tissue ischaemia produced by obstructive arterial diseases a very important reduction of muscle action potentials has been observed, reversible partially after

pharmacological or surgical vasodilation or after administration of various enzymatic high energy rich drugs, such as *cythochrome C*, *phosphorilated sugars*, *various enzymes of respiratory chains*, *ATP*.

The improvement observed, after this pharmacological treatment both of dysmetabolic myopathies and of fatigue and ischaemia condition artificially induced in normal volunteers and again in various neurogenic lesions (acute anterior poliomyelitis, neuropathy of lower limbs) treated with ATP administration to diseased muscles leads the AA. to emphasize the relationship existing between metabolic and electrical activity of muscle fibers and to consider from a pathogenic dynamic (dysmetabolic) point of view the neuromuscular disorders.

RESUMEN

Los autores describen sus hallazgos en estudios electromiográficos de miopatías dismetabólicas, especialmente de enfermedades por intoxicación profesional y por lesiones

arteriales oclusivas de los miembros inferiores.

Los tipos de trazados electromiográficos observados en distintos envenenamientos

profesionales (cambios en los potenciales de acción musculares por intoxicación por monóxido de carbono, reversibles con la vuelta a la oxigenación o después de la administración de enzimas respiratorias; trazados de tipo mixto neurogénico o miogénico, por intoxicación con disulfuro de carbono; de tipo neurogénico por intoxicación por plomo) permiten incluir estos estados mórbidos entre las alteraciones tóxicas dismetabólicas de las fibras musculares.

Se ha observado una reducción muy importante de los potenciales de acción muscular en la isquemia tisular crónica de las enfermedades arteriales obstructivas; la cual es reversible parcialmente después de vasodilatación farmacológica o quirúrgica o des-

pués de la administración de varias drogas enzimáticas de alta energía, tales como *Citocromo C*, *azúcares fosforilados*, *varias enzimas de cadena respiratorias*, *ATP*.

La mejoría observada después de este tratamiento farmacológico, de las miopatías dismetabólicas y en la fatiga y en la isquemia inducida artificialmente en voluntarios normales; así como en distintas lesiones neurológicas (poliomielitis anterior aguda, neuropatía de los miembros inferiores) tratadas con la administración de ATP a músculos enfermos, lleva a los autores a insistir en la relación existente entre la actividad metabólica y eléctrica de las fibras musculares y a considerar de un punto de vista patogénico dinámico (dismetabólico) los desórdenes neuromusculares.

RESUME

Les auteurs décrivent leurs recherches en études électromyographiques de myopathies dysmétaboliques spécialement des maladies par intoxication professionnelle et par des lésions artérielles occlusives des membres inférieurs.

Les types de tracés électromyographiques observés dans différents empoisonnements professionnels (changements dans les potentiels d'action musculaire par intoxication par le monoxide de carbone, réversible au retour à l'oxigenation ou après l'administration d'enzymes respiratoires; tracés du type mixte neurogénique ou myogénique par intoxication avec disulfure de carbone; du type neurogénique par intoxication par plomb) permettent d'ajouter ces états morbides parmi les altérations toxiques dysmétaboliques des fibres musculaires.

On a observé une réduction très importante des potentiels d'action musculaire dans l'ischémie tissulaire chronique des

maladies artérielles obstructives; laquelle est réversible partiellement après la vasodilatation pharmacologique ou chirurgique ou après l'administration de plusieurs drogues enzymatiques de hautes énergies, telles que le cytochrome C, sucres phosphorilés, plusieurs enzymes chaines respiratoires ATP.

L'amélioration observée après ce traitement pharmacologique des myopathies dysmétaboliques et dans la fatigue et dans l'ischémie provoquée artificiellement dans des volontaires normaux; aussi comme dans différentes lésions neurologiques (poliomyélite antérieure aigue, neuropathie des membres inférieures) traitées avec l'administration de ATP à des muscles malades, conduit les auteurs à insister dans la relation existant entre l'activité métabolique et électrique des fibres musculaires et à considérer d'un point de vue pathogénique dynamique (dysmétabolique) les désordres neuromusculaires.

ZUSAMMENFASSUNG

Die Autoren behandeln ihre persönlichen Schlussfolgerungen aus verschiedenen.

Anwendungen des EMG auf dysmetabolische Myopathien, besonders auf die toxi-

schen Berufskrankheiten und die okklusiven arteriellen Erkrankungen der unteren Gliedmassen. Das bei verschiedenen beruflichen Vergiftungen beobachtete EMG (Veraen-

derungen der Potentiale der Muskeltaetigkeit durch akute Kohlenmonoxydvergiftung, die sich normalisieren koennen, wenn die Sauerstoffversorgung wieder in Gang kommt oder nach Verabreichung von Atemfermenten, das EMG gemischter -sowohl neurogener als auch myogener -Natur bei der Vergiftung durch Kohlenbisulfid; das neurogene EMG bei der Bleivergiftung) erlaubt, diese krankhaften Zustaeude den toxischen dysmetabolischen Affektionen der Muskelfasern zuzuordnen.

Im Falle der durch obstruktive arterielle Erkrankungen verursachten chronischen Gewebsischämie hat man eine sehr bedeutende Verminderung der Muskeltaetigkeitspotentiale gefunden, die durch die pharmakologische oder chirurgische Gefaesserweiterung oder durch die Verabreichung verschiedener energiereicher enzymatischer Drogen, wie z.B. des Cytochroms C,

phosphorilisierter uckerarten, verschiedener Fermente der Atmungskette, des ATP, teilweise normalisiert werden koennen. Die beobachtete Besserung nach dieser pharmakologischen Behandlung sowohl der dysmetabolischen Myopathie als auch der Ermuedungs- und ischaemischen Erscheinungen, die bei normalen Freiwilligen kuenstlich hervorgerufen worden sind, und schliesslich auch in verschiedenen neurogenen Krankheitsfaellen (der Poliomyelitis anterior acuta, der Myopathie der unteren Gliedmassen), die mit der Verabreichung von ATP behandelt worden sind, veranlasst die Autoren, die Beziehungen hervorzuheben, die zwischen dem Stoffwechsel und der elektrischen Aktivitaet der Muskelfasern bestehen, und die neuro-muskulaeren Stoeurungen von einem dynamisch- (dysmetabolischen) pathogenetischen Gesichtspunkt aus zu betrachten.

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Electromyographic Findings in Polymyositis

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Between the so-called collagen diseases (C. D.) a singular place is occupied by polymyositis. After the pioneer works of Wagner, Unverricht, Hepp, Jackson, Strümpell and Steiner, the improvement of our diagnostic methods (electrodiagnostic investigations, muscular biopsies) has allowed us to consider this morbid state among the primitive *myopathies*. Fundamental contributions to this subject have been published in the last ten years (Adams, Denny-Brown and Pearson; van Bogaert and Radermecker; Garcin, Lapresle, Gruner et Scherrer; Walton and Adams).

We must distinguish the myositides produced by pathogen noxae of known origin (viral, parasitoxic, piogenous, spirochaetal myositis) from the morbid states we may observe in the course of acute articular rheumatism, of scleroderma, of lupus erythematosus, of panarteritis nodosa.

The purpose of this paper, the description of EMG pattern observed by polymyositis, calls for the sake of clarity, first a brief review of the main clinical patterns of this morbid state, for a correct evaluation of the electrical findings and its importance in the differential diagnosis from the other myopathic states.

Clinical symptomatology of polymyositis

It is very arbitrary to distinguish acute and chronic stages of this disease, but for didactic purpose it is generally accepted to recognize an acute and a chronic course of this morbid state.

In the acute form we observe high fever,

relevant aching of muscles, rigidity of the limbs, rapid involvement of the skin, troubles in deglutition and language, vesical and rectal incontinence, high sedimentation rate, reduction of blood lymphocyte content, with increase of eosinophiles, increase in enzymatic activities, urinary excretion of creatinic compounds, alteration of protydaemic balance. In most cases (70%) we observe a chronic course, with the same, but attenuated, symptomatology: subfebril hyperthermia, involvement of general conditions; atrophy and rigidity of the muscles, circulatory troubles, exanthema with alternative improvement, subcutaneous indurative infiltrations, lesions of mucous membranes with troubles of deglutition and language.

By acute forms we observe generally the coparticipation of scapular girdles and thoracic muscles, in the chronic ones are most evident the weakness. The rigidity of the legs and dorsal muscle. The most striking findings is the spontaneous ache of muscle bells and consequently the painful contracture of these. The participation of tooth, facies, eye and respiratory muscles, as well as of vesical and rectal muscles causes very painful and severe aching. In the cardiac muscle we observe myocardial degeneration foci, evidenced by the EKG with sinusal tachicardia, conduction troubles and arrhythmia, as well as with extrasystoles. Involvement of smooth muscles (esophageal, colon muscles) can be observed, with spastic and atonic troubles, which cause dysphagia, meteorism, constip-

ation, diarrhea, vesical and rectal incontinence.

The polymorph symptomatology of the skin justifies the term, dermatomyositis; we may also observe an involvement of nervous elements, thus neuritic and polyneuritic manifestations (thus the term proposed, polyneuromyositis), with troubles in the tendineous reflexes and general sensibility and pathological responses to electrical stimulation. Strabismus, ptosis, anisocoria, that often complicate the clinical pattern are not of neural, but of muscular origin. Psychically these patients, especially when suffering from dermatomyositis, exhibit drowsiness, preoccupations and depressive states.

The main laboratory findings are the hematological and the enzymological ones. We remember the high increase of leucocytes, with relative lymphocytopenia, high eritrosedimentation rate. Constantly an increase of serum lactic acid can be observed, especially in rest and fasting patients. We have a significant diminution both of serum creatininic and muscle creatine contents. Characteristic changes in serum enzymatic activities can be observed: considerable increase of LDH, SGOT, SGPT, reduction of cholinesterase, for the usure of motor end plates. The alteration of serum proteic balance can be evidenced from eucolloidity tests. By electrophoretic examinations we observe a diminution of serum albumines, with high increase of gamma-globulines, normal values of alpha- and beta-globulines. In chronic states most often we observe an increase of alpha- and beta globulines, a reduction of gamma-globulines; constant urinary findings; of this morbid state is the creatinuria, with values exceeding the 1100 mgr. pro die and high tolerance to creatine surcharge test and total excretion of the administered creatine.

As a consequence of the nervous system involvement we have alterations in cerebrospinal fluid. In the main classifications proposed (van Bogart et Radermecker; Walton & Adams; Garcin et coll.; Coërs, Pruzinsky) the unitary conception dominating these trials is the common histological finding of inflammatory-degenerative lesions of muscular tissue, we

may observe both in polymyositis as well in dermatomyositis.

The frequent observation of a muscular atrophy of various grades in the proximal muscles generates many differential diagnostic problems with muscular progressive dystrophies, especially in chronic cases. Furtado and Alvim have first described the "pseudomyopathic form of polymyositis".

According to various AA., the late myopathic states (*myopathia tarda* of Nevin; *dystrophia musculorum progressiva menopausae* of Shy and Mc Eachern) can be considered as "primitive idiopathic myositis".

Considering the above mentioned difficulties of differential diagnosis, we must now emphasize the aid to clinical semeiology provided by histopathological findings as well as by the electrophysiological investigations (muscle responses to electrical stimulation electromyographic patterns).

According to Hvidt's observations, we could differentiate the "pseudomyopathic forms" of polymyositis from the "dystrophia musculorum progressiva" by these differential signs:

- a) absence of hereditary traits;
- b) uniformity of lesions in both sexes;
- c) involvement of throat musculature and distal muscles of the limbs, with frequent extensive involvement of all muscles;
- d) rapid reduction in muscular strenght;
- e) improvement and, often, complete recovery with treatment. Sarteschi and De Carlo-Giannini have recently reported four cases suffering from polymyositis, with constant paralytico-atrophical patterns of ryzomelic type, slow course, of difficult nosological classification, where the correct diagnosis was reached only with electromyographic and bioptical findings.

The histopathological pattern in polymyositis shows frequent degenerative lesions associated with inflammatory reactions either in connectival, as well as in parenchymal tissue.

Very frequent acute degenerative lesions (fibrocellular necrosis of various degrees) associated with typical myodystrophical lesions can be observed in the same muscular region. The degenerative foci are

frequently surrounded by intensive connective reactions.

In the histological incomplete forms we may find a diffuse oedema (oedematous form of Berguignan) associated with little hemorrhagic infiltrations in the necrotic foci (hemorrhagic form of Marinesco).

The histopathological findings are thus of extreme usefulness for the diagnostic classification of many amyotrophic forms with slow course.

Electrodiagnostic and electromyographic findings in polymyositis

Many EMG observations have been dedicated in the past ten years to the clinical and pathogenetical study of polymyositis. The most important contributions have been carried out by Guy and cow.; Christensen and cow.; Jasper and Ballem; Buchthal and Pinelli; O'Leary, Lambert and Sayre; Grandmaison and cow.; Everett and Curtis; Oester, Rodríguez and Fudema; Thiebaut, Frühling, Rohmer and Isch; Ascione and cow.; Serra and cow.; Antognetti, Scopinaro and Zinolli; De Carlo and cow.; Sarteschi and De Carlo-Giannini; Brumlik and cow.; Girard; Biemond; Howard and Thomas; Boström and Hed; Garcin and cow.; Walton and Adams.

Despite the different histological lesions, the EMG findings of dermatomyositis and polymyositis are very akin.

In polymyositis the mean duration values of action potentials of single motor units are very brief (Buchthal and Pinelli). In the most acute cases no pathological changes from normal values are recorded (Buchthal and Clemmesen); in chronic patients, on the contrary, we frequently observe action potentials of brief duration, probably caused by the increase of propagation of the impulse along the muscular fiber, with reduction of functional length of the fiber.

In dermatomyositic muscles we observe electrical potentials of brief duration, with very sharp spikes of little amplitude. The potentials appear to be polyphasic and very frequently of augmented duration. These potentials, for their little amplitude, are easily differentiated from the reinnervation potentials; for their great duration

are differentiated from the myoatrophic potentials (Guy, Lefebvre, Lérique and Scherrer).

The EMG findings observed by O'Leary, Lambert and Sayre in 45 patients suffering from dermatomyositis showed the following characteristics:

a) prolonged activity from needle insertions, similar to that observed in myotonic and denervated muscles;

b) a persistent electrical activity at rest was observed in 80% of the cases, very difficult to differentiate from fibrillation activity of denervated muscles. This finding is consistent with other electrical patterns of involvement of peripheral nervous system and may probably be caused by the little lesion of the intramuscular nervous fibers;

c) during the voluntary contraction the electrical activity of the muscle appeared to be abnormal, showing frequent action potentials of very short duration and polyphasic type, similar to what we may record from myodystrophic muscles. According to Kugelberg we may suppose by dermatomyositic muscles a volumetric reduction of motor unit. This hypothesis has been very recently confirmed by Buchthal and colls., with the multielectrode techniques. In both myotonic dystrophy and polymyositis the motor unit territory was significantly lower than in a normal muscle, but the maximum voltage was normal (Buchthal, Rosenfalck and Erminio). The increased velocity of propagation of the impulse can also be hypothesized, as Buchthal and Pinelli think.

Very little action potentials, similar to what we may observe by fibrillation activity from denervated muscles, have been recorded of 4 patients suffering from dermatomyositis observed by Oester, Rodríguez and Fudema. This finding was observed at rest, while during the voluntary contraction a wide variety of polyphasic motor units were recorded, frequently with myotonic bursts.

According to these AA. we must differentiate the dermatomyositis patterns from other myopathic muscles (diffuse scleroderma; trichinosis; lupus erythematosus; myasthenia gravis; polyneuritis; thyrotoxicosis and other myopathies)

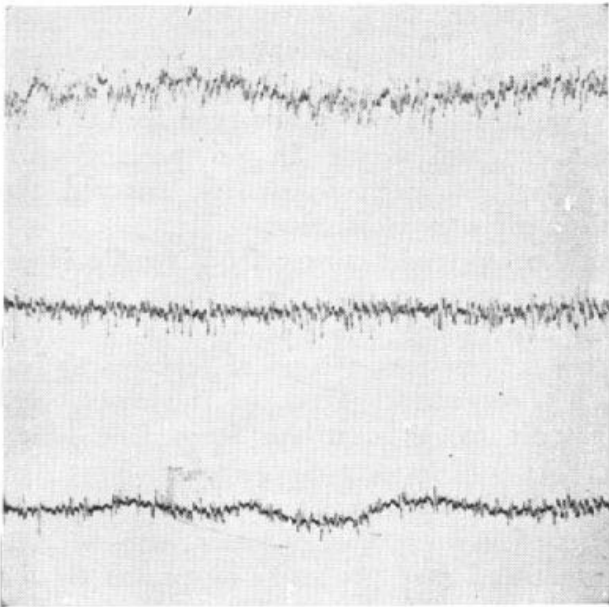


Fig. 1. — *Gastrocnemii* muscles of a polymyositic patient. Positive and "denervated" potentials mixed with "myodystrophic" activity

using as a basis the different EMG findings.

When the clinical involvement is milder, we may observe only polyphasic motor unit. In the most complex cases we can obtain all EMG findings. Very commonly polyphasic or fibrillation potentials have been recorded; we may encounter, in the

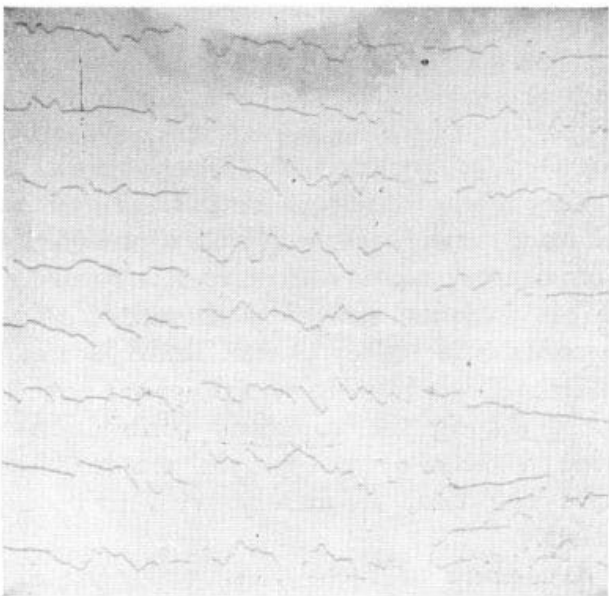


Fig. 2. — Various motor unit potentials of the tricipites muscles of a polymyositis patient. (Amplif. 100 micro V/mm vel.= 1 m/sec.)

same tracing, motor unit potentials of brief duration and little amplitude, during the voluntary contraction, or motor unit potentials spontaneously active. The myotonic reaction is present, in any instances, with motor unit potentials of very little amplitude and very brief duration. According to Oester and cow. we may observe, from the EMG finding, all stages of disintegration and dissociation of the motor unit. The above exposed results are confirmed by Guy's observations and have been very recently observed by Antognetti and cow., De Carlo and cow., Serra and. cow.

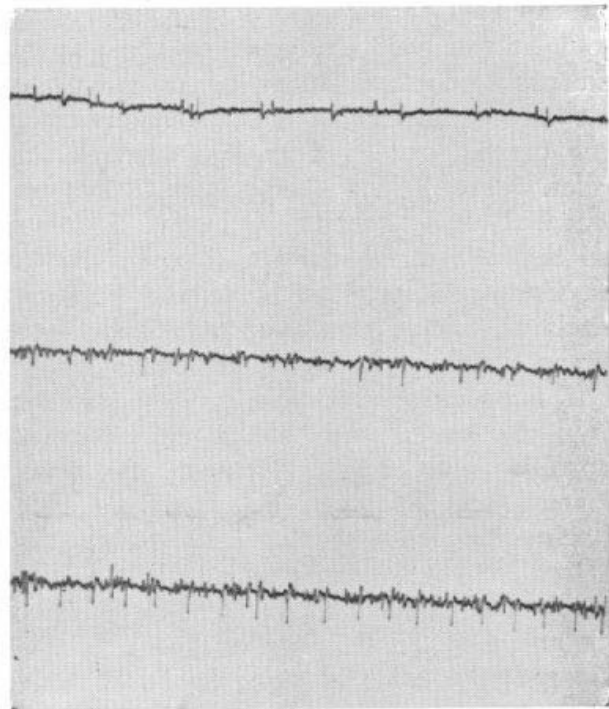


Fig. 3. — *Quadricipites* of a polymyositic patient. Positive sharp waves, mixed with little motor unit potentials of very short duration

The neurogenic pattern may be associated in dermatomyositic and polymyositic muscle with the classical EMG findings of myogenic type, according to the observations of many AA. (Oester and colls.; Richardson; Brumlik and colls.; Serra and colls.) (see figs. 1-2-3) and confirm the clinical transitional forms from dermatomyositis to scleroderma and other collagen diseases observed by various AA. (Brunsting; Pearson; Alanis; Ingrassia and Martelli; Polley and colls.; Calkins and Bauer; Talbott and Ferrandis) De Carlo and colls.

have observed the following EMG characteristics in their polymyositic patients:

a) frequent and intensive insertion activity;

b) spontaneous activity (fibrillatory potentials; "saw tooth potentials" of Jasper; motor unit potentials);

c) significant increase of polyphasic potentials;

d) reduction of mean values of duration and amplitude of single potentials;

e) reduction, during the voluntary contraction, of interference amplitude, proportional to the grade of muscular dystrophy;

f) fiber potentials associated with normal action potentials of motor unit, during the voluntary contraction;

g) bursts of fiber potentials of high frequency both during the contraction as well as during the decontraction after the electrode insertion, the mechanical or the electrical stimulation ("pseudomyotonic" or "myotonoid" discharges).

The recent observations by Thiebaut, Frühling, Rohmer and Isch of a patient with pseudomyopathic polymyositis and EMG histological findings typical for myodystrophic muscles and a patient suffering from typical dermatomyositis with undulatory course, clinical improvement and persistent muscle histological and bio-electrical lesions confirm also the possible transitional forms from one to another morbid state. In the observations of the French AA, the EMG exhibited a very polymorph pattern, with motor unit potentials of brief duration and polyphasic type in the most cases. From any muscles the tracing were of "symplex" type. According to the Strasbourgean electromyographers the most striking finding in these tracing consisted of low oscillations of elevated frequency, modulated with frequent little spikes, a pathognomonic finding of this morbid state.

In recent observations of Italian AA. (Antognetti and colls.; De Carlo and colls.; Serra and colls., Sarteschi and colls.) from viral myositis and polymiositis the EMG findings are very similar to the myoelectrical signs of muscular dystrophia. The EMG characteristic of these inflammatory diseases consisted in the diminution of mean duration of muscle action potentials, whilst

the mean amplitude values were borderline and a frequent incidence of polyphasic potentials could be evidenced. Beside these findings of "myogenic" type, other electrical signs, of "neurogenic" type, could be very frequently recorded: fibrillation potentials at rest (Bauwens, Guy and colls; Richardson) or after the insertion of needle and mechanical stimulation (Pinelli; Pinelli and Ghisoni). These findings have been accounted for the direct irritation on the muscle by the inflammatory lesions (changes in electrolytic balance, mechanical compression by the oedema) or for the simultaneous involvement of the intramuscular nervous fibers. With the faradic subwedensian stimulation no repetitive responses have been observed in these instances, that confirms the myotonic component in the myositic pattern. We observe furthermore a reduction both of interference amplitude, during the voluntary contraction, and the evoked potential from nerve stimulation (Pinelli). A tendency to galvanotonus, with increase of chronaximetric values (Guy, Lefebure, and Scherrer), has also been observed. The presence of striking signs of "neurogenic" type, as well as of "myasthenic" patterns have been very frequently stressed (Bonduelle and colls.).

The "strength-duration" curves, as results from Richardson's and Walton's studies, show the "denervated" state, confirming the concept of "neuromyositis". As was stressed by Walton the "denervation" is almost complete, when we judge the results of these electrophysiological investigations. We may suppose, according to Richardson's thinking, that the polymyositic process leads to involvement of the intramuscular nervous fibers, sparing the motor end plates and the nervous conduction in the proximal segment of the nerve. The chronaximetric findings, as reported by van Bogaert and Radermecker; Bourguignon C. and Bourguignon A., in the polymyositic muscles, showed an increase of chronaxic values at rest and a great variability of mean chronaximetric values from the same muscle, with signs of fatigue greater than we may observe in myasthenic muscles. The increase of vestibular chronaxic values demonstrates the central mechanism to be very probable

DIFFERENTIAL DIAGNOSTIC FEATURES								
MORBID STATE	INSERTION ACTIVITY	SPONTANEOUS ACTIVITY	POTENTIAL DURATION	POTENTIAL AMPLITUDE	POLYPHASIC POTENTIALS	MAXIMAL CONTRACTION	MYOTONIC ACTIVITY	MOTOR UNIT TERRITORY
POLYMYOSITIS	Vivacious and prolonged	Fibrill. Potentials; "saw tooth pot."; motor unit potent.	Reduction of mean values	Reduction of mean values	highly increased	reduction of interference fiber potentials	"pseudo-myotonic" discharges	reduction: Normal fiber density
MUSCULAR DYSTROPHY	—	—	Reduction of mean values	Reduction of mean values	significantly increased	Reduction of interference amplitude	—	Reduction of average motor unit territory and fiber density
NEUROPATHY	Significant	Significantly increased	increase of mean values	Increase of mean values	increased	reduction or absence of interference pattern	—	increased
MYOTONIA	Significant and prolonged	—	Normal values	Normal values	—	slightly reduce	characteristic myotonic discharges	Reduction of average motor unit territory; same fiber density as in normal muscles

in pathogenesis of dermatomyositis as well of other collagen diseases. The importance of this pathogenetical role has been also stressed by Serra and colls., in their comparative EEG and EMG studies of collagen diseases, with the frequent finding, in dermatomyositis as well as in other morbid states of a neuronically labile evidenced by intermittent photic stimulation (slow bilateral, asynchronous waves) indicative of general neuronically involvement, as emphasized also by Krump (see figs. 4-5).

We may summarize the main EMG findings by polymyositis in the following table.

DISCUSSION

The EMG tracing of polymyositis patients appears to be a very complex pattern, resulting from the association of bioelectrical signs accounted for myogenic lesions with myoelectrical findings typical for the neurogenic lesions. We must now evaluate the clinical and pathogenetical meaning of these features, considering our recent knowledge upon the biochemical and histopathological findings of myopathies.

None of single EMG findings of polymyositis is itself pathognomonic of this morbid state, but the complex association of various signs may help in the diagnostic task of this collagen disease against other myopathies. (See above *Table*.)

The diminution of average duration of action potentials, a very common finding of polymyositis, is absolutely non-specific, because we may encounter these findings also in muscular dystrophy; more significant is the concordance of this signs with other EMG findings.

The presence of "fiber potentials" is not a synonymus of denervation, because we may record this tracing from non-neurogenic myopathies, especially from polymyositis.

According to De Carlo's observations, the motor unit can show a functional fragmentation with partial contraction:

a) when a portion of M. U. is wasted (polymyositis; dystrophia musculorum progressiva);

b) when the fibers are abnormally excitable and escape to the axonic subordination

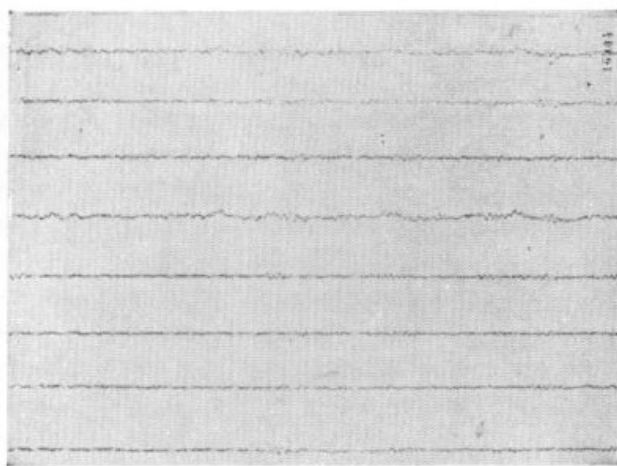


Fig. 4. — *Borderline ground activity from a patient with diffuse polymyositis*

ion, that leads to spontaneous and anarchistic contraction (myotonia; polymyositis);

c) for an alteration of the nervous regulation (denervated activity).

The myotonic discharges very frequently observed by polymyositis are bursts of "fiber potentials" and may be recorded in all conditions of altered excitability cycle of the fibers that lead to iterative paroxysm of the contraction. This is the meaning of the *insertion activity*, for the abnormal excitability or irritability. This finding is very consistent in polymyositis.

The "saw tooth potentials" described by Jasper are the most non-specific signs of suffering of muscle fibers. The significant frequency of this finding in polymyositis tracing is a very important feature for the diagnostic evaluation (Parma and colls.).

The reduction of mean values both of duration and amplitude of action potentials cannot be accounted for dystrophia muscul. progressiva, for the coexistence of the fiber potentials and other signs of abnormal excitability.

These fiber potentials, on the other hand, cannot mean a trouble in nerve conduction, owing to the reduction of mean values of duration of single action potentials, a finding non consistent with the nerve lesions.

The fiber potentials in polymyositis are also recorded during the contraction, whilst in "denervation" this finding can be observed only at rest.

This complex picture of the EMG tracing of polymyositis is very probably accounted

for by the heterogeneous and complex lesions typical of this mesenchimopathy.

The above described EMG findings, considered as a whole, cannot be confused with other myopathic tracings. This individuality can be easily understood, considering both the biological and histopathological lesions of this morbid state.

As results from numerous histopathological studies (Adams, Denny-Brown & Pearson; Buchthal and colls.; O'Leary and colls.; Sarteschi and De Carlo-Giannini; Walton and Adams) the histologic changes can explain the EMG picture. The loss of muscle fibers according to Buchthal's observations, can be accounted for the reduction of motor unit territory, as well as for the amplitude of the spikes, their reduced average duration and finally for the increased incidence of polyphasic potentials. In polymyositis, as well as in the pseudohypertrophic type of dystrophia musculorum progressiva Buchthal and colls. attribute the short duration of action potentials to the absence of the initial and terminal low voltage components of motor unit potentials. Coërs and Woolf have histologically proved the peripheral sprouting in these morbid states, responsible for the increased number of fibers per subunit and the normal maximum voltage (Buchthal and colls.). On the other hand the localized peripheral sprouting does not cause an increased extent of end plate zone, affecting therefore the average duration of action potential (Coërs & Woolf).

The enzymatic features and other bio-

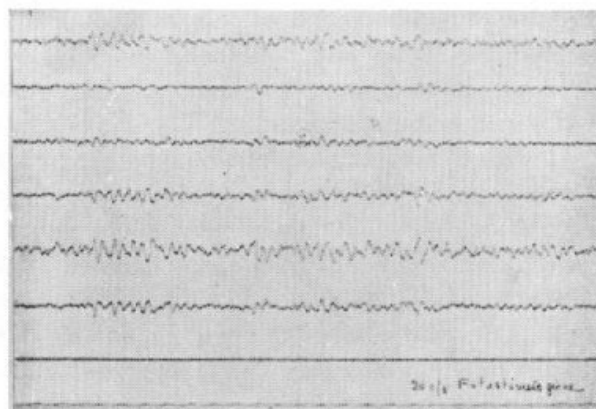


Fig. 5. — *Pathological responsivity of electrical activity to intermittent photic stimulation by the same patients of fig. 4*

logical changes in polymyositis can be, on the other hand, responsible for mioelectrical signs.

The electrolyte balance can show significant changes, accounted very frequently by the pathogenesis of polymyositis. We remember, for example, the observation of Alanis and Flanagan of a myopathy associated with hypercalcemia, occurring with carcinoma of the kidney. The improvement of dermatomyositis after the treatment with Sodium-EDTA leads also to emphasize the importance of changes in mineral metabolism for the pathogenesis of dermatomyositis (Pollock). The influence of potassium and other ions on the membrane potential of single muscle fibers was experimentally demonstrated by Hodgkin and others. Serra, on the other hand, has frequently stressed the importance of "metabolic periphery" for the muscular electrogenesis.

As results from experimental studies of Maeda and Dogura, the growth of staphylococcus bacteria adapted to muscle extracts was accelerated by extracts of skeletal muscle whereas smooth muscle extracts inhibited growth. Lecithinase activity and P^{32} uptake in the ribonucleic acid of the cell body of bacteria, which had been adapted to either bone marrow or muscle, were also increased by skeletal muscle and bone marrow extracts. The ATQ-ase activity of staphylococcus strains adapted to skeletal muscle extracts was only activated by the addition of the non-dialysable part of a muscle extract. Probably myosin may be the activating factor. Likewise, the strong alkaline phosphatase activity of bone marrow-adapted bacteria was increased by the addition of bone marrow extracts, especially by the metaphysial extracts. The importance of these findings for the pathogenesis of polymyositis and osteomyelitis can thus be stressed.

The electrophoretic studies carried out by Buscaino G. A. and Corsi of the muscle proteins in subjects suffering from various neuromuscular diseases has demonstrated, in polymyositis as well as in other myopathies, very interesting pathological findings. The high and low ionic strength extracts prepared from muscle fragments from 24 patients suffering from various neuromus-

cular affections were subject to electrophoresis and exhibited decrease of myosin and actomyosin content, with relative increase of γ -myosin, increase of Jacob's group III (myo-albumin), and, less frequently, decrease of the rapid component of Jacob's group I with increase of the slower component. The ratio of myogen to myosin and actomyosin content was mostly increased. The degree of functional and anatomical disturbance and of electrophoretic changes seemed to be proportional. According to Buscaino's findings, the increase of Jacob's group III is roughly proportional to the amount of connective tissue, as estimated by microscopical examination. The group III can be associated, partially or totally, with the albumins of interstitial connective tissue. The elevation of gamma-globulines in acute dermatomyositis was also observed by Teodorescu and Dumitriu.

The interferences of exosaphosphates and creatinic metabolism in myopathic patients, as stressed recently by Bertolini and Riva, Minazzi and others, can also be considered as responsible for the pathogenesis of bioelectrical signs.

The glutamic oxalacetic transaminase activity of the serum in polymyositis can be normal in childhood and allows to differentiate this collagen disease from Duchenne's type of dystrophia musculorum progressiva (Murphy & Cherniak). This enzymatic activity was found to be increased in adult's dermatomyositis and polymyositis.

The importance of serum enzymes in muscular physiopathology, as stressed by Dreyfus and Schapira, may also be accepted in pathogenetical interpretation of EMG findings in polymyositis.

The increase in serum enzymes activity, (especially hyperaldolasemia) in this myopathy can be, as it was demonstrated for dystrophia musculorum progressiva, of muscular origin. The trouble of muscular permeability, for the histological lesions typical of polymyositis, or the rate of synthesis or degradation of muscle proteins (see Buscaino's findings) can be accounted for by the mechanism of changes in serum enzymes and muscle enzymes observed in polymyositis patients.

As concerns the frequent association of dermatomyositis or polymyositis with neoplasia of various organs (Williams; Hegglin and Siegenthaler; Atsmon, Shibolet & Kessler; López García and cow.; Goldfischer and Rubin; Garde, Aymard and Tommasi; Zinoli and cow.; Garcin and cow.) it has been stressed, beside the most common pathogenetical mechanisms (neurogenous, dysvitaminosis, dysenzimopathic), the importance of toxic or dysmetabolic troubles associated with the tumoral lesions. According to Henson's observations, the neuromuscular lesions could be pathogenetically connected with the yet unknown cause of carcinogenesis. Finally we must stress the good therapeutical results observed with various steroid treatments (Lushnikova, Finzi and Pirinisi; Kirschbaum; De Rosa; Bajusz; Bureau and cow.; De Carlo and cow.; Sarteschi and De Carlo-Giannini) that may be interpreted as an authoritative confirmation of flogistic components in polymyositis lesions.

The association of such a disease with

other collagenopathies, as results from the observations of various AA., the cutaneous disorder of connective tissue very frequently (60% of the cases) observed in amyotrophic lateral sclerosis (Fullmer, Siedler, Krooth and Kurland), the frequent incidence of calcinosis in dermatomyositis; the retinal lesions scarcely observed in association with dermatomyositis (Delogu and other AA.), the probable vascular component in polyneuropathic and polymyositis (Kalm and Seitz) and finally the possible role of hereditary components in the pathogenesis of dermatomyositis, polymyositis and other collagen diseases (Mc Kusick and others) explain the complexity of various problems, either from the anatomoclinical, as well as from the biological and electrophysiological point of view, connected with the polymyositis group and emphasize further more the good diagnostic aid of various electrodiagnostic investigations, especially of electromyography for the pathogenetical meaning and the nosographical classification and differentiation of polymyositis.

SUMMARY

After the review of main clinical and histopathological features of polymyositis, the complex electromyographic patterns from polymyositis muscles and the responses of muscle fibers to nerve stimulation are briefly exposed; both the spontaneous and the evoked electromyograms are consistent either with a primitive involvement of muscle fibers as well as with a nervous damage, as it has been frequently observed by various AA. and results from comparative EEG and EMG studies

in this morbid state and in other collagen diseases.

The diagnostic aid for differentiating the polymyositis from other myopathies is stressed and the various electrical signs are discussed, starting from the histological and biochemical findings observed by this collagen disease.

The importance of troubles in enzymic muscle activity and in protein synthesis for the genesis of electrical alterations recorded by polymyositis is emphasized.

RESUMEN

Después de ser expuestas las principales manifestaciones anatómicas de la poliomiositis y las dificultades del diagnóstico diferencial entre la poliomiositis y las otras miopatías, se subraya la gran utilidad de los datos electromiográficos que resultan de la repercusión simultánea del sector muscular y del nervioso de la unidad neuromotriz.

Al aprovecharse estos datos y los resultados de los exámenes histológicos quedamos en posesión de elementos preciosos para la ubicación nosográfica de las poliomiositis.

La discusión de los datos electrofisiológicos nos conduce a subrayar la importancia de las alteraciones de las actividades enzimáticas del suero y de las proteínas del músculo.

RESUME

Après l'exposition des données anatomo-cliniques observées dans la polymyosite et des difficultés diagnostico-différentielles entre la polymyosite et autres myopathies on souligne la grande utilité des données électromyographiques, résultant d'un réentissement simultané de la portion "myogène" et de la portion "neurogène" de l'unité neuro-motrice.

L'utilisation de ces données et des résultats des examens histologiques nous donne des renseignements précieuses pour l'encadrement nosographique des polymyosites.

La discussion des données électrophysiologiques nous porte à souligner l'importance des altérations des activités enzymatiques du sérum et des protéines du muscle.

ZUSAMMENFASSUNG

Es wird an das klinische und anatomopathologische Bild der Polymyositiden kurzlich erinnert, um die grossen differentialdiagnostischen Schwierigkeiten dieser Krankheit gegen die anderen Myopathien zu neberwinden.

Die elektromyographischen Befunde, die bei den Polymyositid beobachtet werden,

sind für eine gleichzeitige neurogene und myogene Laesion charakteristisch.

Die kritische Auswertung solcher Befunde lässt die Meinung sehr wahrscheinlich sein, dass die Veränderungen der enzymatischen Muskelaktivität, sowie der Muskelproteine für die meisten elektromyographischen Zeichen verantwortlich sind, die bei dieser Krankheit beobachtet werden.

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Personality

Prof. Dr. HENRY ALSOP RILEY

Strange thing vocation: That inner voice ruling our life can't go unheeded without the risk of a frustrated existence.

Sometimes, vocation is deeply hidden in our unconscious mind, and requires an exploratory survey to get acquainted with it. Sometimes, it rings clear since childhood. So, it happened with Dr. Riley. When asked if his parents had any influence on his chosen career he answered us



"I am not sure whether my parents had any influence on my decision to become a doctor, because I never thought of doing anything except being a doctor. One of the stories that my mother told me was that at the age of four, when I was asked what I was going to do when I grow up, I said that I was going to be a doctor in order 'to make people well'".

As the years passed by, the child's wish became a prophetic one. Many lives have been saved, by this thoughtful physician, who devoted his own to the service of suffering mankind.

Today Doctor Riley is considered one the world authorities in our speciality, and his name is linked by honorary degrees with many Societies of different countries.

Taking up the thread of his story we will return to his childhood. His father Henry August Riley, was a lawyer and died when Henry was only 5 years old. He has only a vague idea of his father and can hardly remember him at all. Maybe he inherited his vocation along with the same name, from his grandfather, Henry Alsop Riley, a physician, a Catholic priest and finally a Presbyterian minister in Northern Pennsylvania.

His maternal grandfather was a business man connected with the old Dams Express Company and came from Maine. His maternal ancestors lived in New York since the early 1800's.

Three women looked after him in his early years, his grandmother, Mrs. Erastus Littlefield his mother Mrs. Mariana L. Riley and his aunt, Miss Harriet S. Littlefield.

His student days at Yale passed without stirring the hidden fire of enthusiasm and dedication.

Like many others at his age, he only concentrated on those subjects that appealed to him, in his case biology and comparative anatomy. So he didn't stand particularly well scholastically. He confessed "I didn't appreciate the value of hard work".

But what a difference when he began his medical studies at Columbia University! He felt suddenly plunged into an atmosphere of intense competition, nearly one hundred students struggling to learn and to stand above the average. This along with the healthy influence of outstanding teachers, spurred him on to deeper and more eager study. The fire of enthusiasm was lighted and never more was to diminish during his life. Soon came the reward. The student Henry Alsop Riley graduated at the head of his class and had the highest standing in the Hospital graduates' examination, which at that time included oral and written examinations on the house staff of Presbyterian, Roosevelt and New York Hospital.

There is not a "self made man" that has not shared his task with many others. Like a mosaic, every outstanding teacher leaves a bit of truth in our lives, which all together, makes up the rich pattern of knowledge.

The most rewarding experience about searching the why and how of any life crowned with success is to discover the summing up of many others hidden in his memory and subconsciously exercising their healthy influence. So, when Prof. Riley talks about the days in the College of Physicians and Surgeons, the names of such outstanding specialists as M. Allen Starr, Charles L. Dana, J. Ramsay Hunt, and Frederick Peterson come to his lips.

We think of the stimulating atmosphere that those masters of neurology must have exercised on the young specialists of that epoch.

It would seem strange for those physicians who are at present receiving their training in neurology at Columbia University Hospital to think about the time when neurology was in its pioneering days.

Although they were highly qualified teachers, the courses of neurology were entirely confined to didactic lectures and clinics because there was not a University Hospital at that time and no neurological service was connected with the Department of Neurology at the College of Physicians and Surgeons.

At the time of the first world war in the teaching and military administration of the New York Neurological Schools, Dr. Riley came in close contact with Charles A. Elsberg. This noted neurosurgeon was very anxious to win Dr. Riley over to the field of Neurosurgery, but this didn't appeal to him so much as neurology itself, and besides the technical side of surgery didn't interest him at all.

At that time Dr. Riley's contacts outside the New York Neurological

Institute were with Charles L. Dana, Bernard Sachs, Israel Strauss, Isador Abramson, and chief of them all Frederick Tilney. The most important element in his decision to go into neurology was his contacts with the latter and Herman V. Schulte, who were working in the Department of Anatomy under the direction of Charles S. Huntington, one of the foremost morphologists in the United States.

Dr. Schulte was interested in the nervous system from the morphological and embryological point of view.

Dr. Tilney shared this interest with him and also that of comparative neurological anatomy, but he was also an active practitioner of neurology. During the year that Dr. Riley was in the P. and S. Dr. Tilney took him on several occasions to see and examine neurological patients in the wards of the Kings County Hospital in Brooklyn, where he was a member of the attending staff.

The need to earn his living was solved by a proposal of Dr. Tilney to assist him in his office. There a great mass of neurological patients filed through in the ten years of his close association with Dr. Tilney and thus gave him a solid clinical experience.

There was no doubt that Dr. Tilney was the predominant influence which moulded Dr. Riley as a young physician.

The influence of Schulte and Tilney was evident through the interest Dr. Riley has always shown toward the morphology of the central nervous system. The fact that Dr. Riley has been always in active practice prevented him from devoting full-time attention to any extensive or intensive neurological investigations, but he has published a considerable number of clinical papers on neurological and allied subjects. He was co-author with Frederick Tilney in the preparation of "Forms and Functions of the Central Nervous System" and the author of the "Atlas of the Basal Ganglia, Brain Stem and Spinal Cord".

Concerning his Texas Border war experiences during 1916, Dr. Riley recalled that he was in the General Medical and Surgical Service of the 3rd Ambulance Company and the Camp Hospital of the 27th Division at McAllen, Texas. The only impressive clinical experience which was much out of the ordinary course of military service, was the very extensive epidemic of paratyphoid fever which broke out among the U.S. troops stationed along the Rio Grande. They had been immunized only against typhoid fever and there were hundreds of cases of paratyphoid A and B which passed through his ward in the Camp Hospital at McAllen on their way to the base Hospital at Houston, Texas. The main thing that Dr. Riley remembers about the Mexican Border services, was the mud, torrential rainstorms, temperatures in the summer up to 115°, and every form of discomfort that can be imagined. (It seems discouraging, doesn't it?).

In World War I, Dr. Riley was battalion surgeon of the 105th Machine Gun Battalion and was responsible for the cases of minor surgery and all illnesses of lesser importance in the Machine Gun Battalion medical headquarters at Camp Wadsworth, New York. His connection with the active military forces was terminated by his assignment to the Second New York Neurosurgical School, and he was appointed as the Adjutant

of the Third and Fourth Neurosurgical Schools which were continued until the end of the war toward the end of 1918. He was then discharged and resumed his association with Dr. Tilney and the Neurological Department of the College of Physicians and Surgeons.

Later, as the Assistant Secretary and then Secretary of the American Neurological Association for twenty-five years, he came into contact with all or the foremost neurologists and neurological surgeons who served as Presidents of that Association. Among these were Hugh T. Patrick of Chicago, Elsberg, Mills Spiller, Weisenburg and Dercum of Philadelphia, and Schwab of St. Louis.

Besides getting acquainted with these big names in Neurology, Dr. Riley enjoyed the privilege of getting to know a team of younger specialists who were working with them and building up their own practices and projects of investigation. As it was already stated there was a Department of Neurology under M. Allen Starr when Dr. Riley was in the P. and S. and at the Presbyterian Hospital. Prof. Starr resigned about 1916 as Professor of Neurology and Prof. Tilney was appointed Professor of Neurology. Clinical facilities were added to the Department of Neurology at Columbia, by its affiliation with the Neurological Institute in about 1918, and at that time the heads of services were such famous names in the history of American Neurology as Drs. Tilney, Foster Kennedy, Edwin G. Zabriskie, Walter Timme.

The neurological surgeon was the equally renowned Dr. Charles A. Elsberg. Dr. Riley was in close contact with all of them as he was at that time Secretary of the Medical Board of the Neurological Institute.

Until 1927, Dr. Riley did not have personal contact with neurologists outside the United States but in 1927 a joint meeting was held in London of the neurological section of the Royal Society of Medicine of England and the American Neurological Association. Dr. Riley attended this meeting as Secretary of the American Neurological Association, and at that time he made life-long friendships with Gordon Holmes, Kinnier Wilson, Sherrington, Purver-Stewart, Walshe, and many others belonging to the younger generation. As a result of this meeting Dr. Riley's friendships were strengthened by contacts with the neurologists of the world in the series of International Congresses.

Today neurologists are accustomed to attending International Neurological Congresses, where specialists from practically all of the countries of the world join together to discuss subjects of common interest. In these Congresses there are no lines of separation or frontiers of race or color. This is so natural now that attending specialists never give a thought to how such international conferences came about.

It is of interest to trace the course of events which led to the organization of the International Neurological Congress. In the summer of 1927, two neurologists met at Bad Gastein, as had been their custom for many years, an American, Bernard or "Barney" Sachs as he was affectionally called in American and an Austrian, Otto Marburg of Vienna. During these days of rest and comradeship there began to germinate in their minds an idea of creating a meeting that would have a real

international character. This idea was discussed and approved at the next meeting of the A.N.A. and there then began the history of the International Congresses of Neurology.

Barney Sachs was appointed president of a committee dealing with international neurological activities of the A.N.A. Dr. Riley, the secretary of the A.N.A. was appointed as secretary of this committee of the A.N.A., thus associating him with the Congress from its very origin. Two years of intense activity with correspondence being established with all the groups of neurologists throughout the world followed the appointment of this committee and in Berne in 1929 a meeting of a Program-Executive Committee, consisting of representatives of many countries was held and Dr. Sachs was elected President of the First International Neurological Congress and Dr. Riley was elected as the General Secretary, with Charles DuBois of Berne as the local Secretary.

At this Program-Executive Committee meeting, the general principles of the early Congresses were set up and all of the necessary local arrangements were taken care of.

This first and historical Congress was held in Berne in 1931 and made noteworthy by the attendance of personalities of world wide fame, such as Sherrington, Kinnier Wilson, Gordon Holmes, Guillain, Henri Claude, Nonne, Bing Marburg, Rossi, Ariëns Kappers, Wimmer, Monrad-Krohn, Krabbe and many others.

In 1931 all expectations were surpassed by the success of the first International Congress of Neurology held in Berna, which began in an enthusiastic atmosphere. Not only did the above mentioned personalities attend but many others came anxious to benefit from this exchange of knowledge drawn from their vast experiences.

Among them came the well known Russian neurophysiologist Pavlov, whose reputation had spread beyond his country's confines and had won the respect of the rest of the world.

Several Congresses have been held following the same pattern as the first, one. Soon these meetings became the most important event in world neurological life.

The second took place in London in 1935 and the third in Copenhagen in 1939.

The shadows of the Second World War were like a menacing cloud forecasting a storm for many nations and gave an atmosphere of uneasiness to this Meeting.

The threatening gestures against Poland forced the scientists of this country to leave the meeting, and they were followed by the English and the Dutch neurologists.

All this upset the programme of the Congress.

Happily everyone of the neurologists reached their homeland safely. Dr. Riley decided to go ahead with the vacation itinerary and visited Sweden and Norway leaving this country from Bergen one day after the Athenia was sunk.

Dr. Riley remembered that this event made everyone on board ship afraid and jittery the whole journey.

The war brought a dramatic close to these meetings. Scientific gatherings are a luxury only possible in peace time.

Once the trouble was over, the Congress began anew and as Dr. Riley proposed in 1939 in Copenhagen the 1947 Program-Executive Committee Meeting and in 1949 the Fourth International Congress were held in Paris, Prof. Raymond Garcin acting as General Secretary and employing his effective efficiency and his well known friendliness to their fullest extent.

From the very beginning until today Dr. Riley has been a living symbol of the International Congress of Neurology, his presence is surrounded by the affection and esteem of all the members. He is the only one of the initial Berne group who has continued to work actively.

He has been appointed Vicepresident for the United States Neurologists to every one of the International Congresses of Neurology up to the Congress in Brussels, then he was elected as an Honorary President of the Congress. Dr. Riley has always guided and protected the better development of the International Neurological Congresses, and his rectitude and greatness of soul exercise a healthy influence giving to these meetings an atmosphere of real democracy in the world of Science.

Talking about Dr. Riley with several of the young neurologists that are in the vanguard of today's neurology, they all expressed respect and affection toward him, and referred to him saying "He is a real gentleman".

And he is in every sense of the word. His friendliness his amability and his thoughtfulness which everyone has experienced in his company, has won for him friendship from all over the world. He has won the admiration of all for the courage he has for his convictions.

He is the symbol of the American spirit at its best.

VICTOR SORIANO

• Book Reviews

**"Elettromiografia clinica". - Quaderni di
"Acta Neurologica" - by Carlo Serra,
Lucio Covello - 507 pp. Naples 1959.**

The numerous clinical applications of the EMG, that the authors divide according to the different specialities (neuropsychiatry, neurosurgery, orthopedia, internal medicine, dermatology, ophthalmology, kinesiology, otorrinolaringology) are illustrated with many pictures, obtained above all from their personal experiences.

Its two first parts are devoted to the neurophysiological basis, biochemical, anatomical and functional and to the electromyographic techniques. The third part that embraces the clinical indications above mentioned, begins with a chapter dedicated to the most modern clinical and biological concepts about myopathy.

The latter serves as a useful introduction to the description of so vast and specialized subjects, that is explored in the last nine chapters.

Very rich in bibliographical data (1133

citations classified according to a rigid analytical criterion).

This book also contains an alphabetical index and of authors that very much facilitates consultation.

With the latest developments, the contents follow the principles of the school to which both authors belong. The graphs are not considered as a mathematical recording without semantic value, but as an expression of the cells life itself.

This book on electromiography, fills a gap in the world literature and represents the first attempt bring together in a complete whole the numerous but dispersed contributions.

In this way the muscular activity is represented as the harmonic fusion of the central and peripheric impulses, above all of that "metabolic peripheric" these conclusions are based on exhaustive clinical and experimental investigations by the two authors.

All throughout this book this fact can be observed, and its reading really interesting as well as instructive for everyone engaged in "true investigation" in any field of medical science.

• News

SOCIÉTÉ FRANÇAISE DE BIOLOGIE MÉDICALE

Président: Pr. R. Fauvert, Hôpital Beaujon-Clichy; *Secrétaires:* Dr. M. Lamotte, 48, rue du Dr. Blanche, Paris-16; Dr. M. Boiron, 22, avenue Victoria, Paris-4; *Trésorier:* Dr. F. Poutrel, 43, rue Sahel, Paris-12.

JOURNÉE DE BIOLOGIE MÉDICALE du Dimanche 20 Novembre 1960

Hospice de la Salpêtrière, École des
Infirmières

47, Boulevard de L'Hospital, Paris 13

P R O G R A M M E

SALLE 1: *Colloque sur la Myasthénie,*
sous la Présidence du Professeur P. Mollaret.
de 9 h. à 12 h. 30: Introduction par le
Professeur P. Mollaret; Docteur Couteaux

et collab. Données pharmacodynamiques des anticholinestérasiques; Docteur J. J. Pocard. Données pharmacodynamiques des anticholinestérasiques; Professeur agrégé Scherrer et collab. Données électrophysiologiques sur le muscle myasthénique; Docteur M. Goulon. Traitement médical et réanimation; Professeur L. Léger. Traitement chirurgical.

SYMPOSIUM TO BE HELD ON CEREBRAL LIPIDOSES

A joint announcement has been made of plans for a proposed Symposium on the Sphingolipidoses and Allied Diseases to be held March 29-30, 1961 by the three sponsoring organizations — Isaac Albert Research Institute of the Jewish Chronic Di-

sease Hospital, Brooklyn; State University of New York, Downstate Medical Center, Brooklyn; National Tay-Sachs Association, New York.

The two-day conference will be held at the Isaac Albert Research Institute and the Downstate Medical Center.

Distinguished scientists representing leading American and West European universities and medical centers are expected to attend. The conferees will offer a summation of their findings regarding these diseases. Tay-Sachs' Disease and allied fatal degenerative diseases of the nervous system occurring in infancy and childhood. This multi-disciplinary approach will include pertinent studies in the biochemistry, histochemistry, neuropathology, electron microscopy, and genetics of the sphingolipidoses.

There will also be a summation of studies in the emotional and psychological effect on family living habits resulting out of the occurrence of these fatal diseases within the family group.

Investigators interested in attending or participating in the symposium should write to: Director, Isaac Albert Research Institute, Rutland Road and East 49th Street, Brooklyn 3, N. Y.

SYMPOSIUM ON THE OCULOMOTOR SYSTEM

ABRIL 14 - 15

Sponsored by U.S.P.H. at the Mt. Sinai Hospital, New York City

The objectives of the conference are:

1. To accumulate and correlate data for use as a source of reference for those engaged in anatomic, physiologic, neurologic,

ophthalmologic and otologic research, with particular reference to the oculomotor apparatus.

2. To stimulate interest in the study of the oculomotor system against a background of the known facts obtained in research of postural mechanisms, as well as visual and vestibular systems.

3. To point out the gaps in our knowledge of the various systems, with particular emphasis on the inter-relationships between the oculomotor, vestibular and visual systems.

The topics to be considered at the meeting are as follows:

1. The anatomy of the oculomotor pathways in the cerebrum and brain stem, ocular nerves and muscles.

2. The physiology of oculomotor pathways based on experiments dealing with electric stimulation, electrical recording and the effect of lesion in the anesthetized and unanesthetized preparation, using implanted electrodes.

3. The pathology of oculomotor system. This topic may be covered by clinicopathological correlations in man.

4. The role of vision in oculomotor performance. The inter-relationship between the visual and oculomotor processes. The influence of vision on eye movements. Visual-ocular integrations.

5. The influence of the vestibular and tonic neck impulses on the oculomotor system. Vestibulo-ocular integrations.

6. The inter-relationship between the oculomotor and other systems. Postural mechanisms. Sensory-ocular integrations. Psychological influence on oculomotor functions.