Summary

Twenty-seven vesico-vaginal fistulae are presented. Cephalopelvic disproportion is shown to play an important part in their causation.

Treatment was by vaginal repair in 17 cases, transplantation of the ureters in four, and reconstruction of the anus with closure of the vaginal introitus in one case. Three patients left hospital before their treatment was finished, and the completion of treatment was not seen in two cases.

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SERUM ELECTROPHORETIC CHANGES IN POLYMYOSITIS

BY

KETTY GAVRILESCU,* B.Sc.
Dip.Med.Chem.(Buch.), F.I.C.(Buch.)
Senior Biochemist

J. MICHAEL SMALL, M.B., B.S., M.R.C.P.
Late R.M.O., Maida Vale Hospital

From the Department of Pathology, Maida Vale Hospital for Nervous Diseases, London

The diagnosis of muscle disorders is ever a difficult clinical problem, and, even with the aid of a muscle biopsy, electromyography, and appropriate biochemical tests, the clinician may be forced to accept the unsatisfactory label of a "myopathy of undetermined aetiology."

Walker and Benditt (1950) and van Sande (1954) have suggested that serum electrophoresis is of value in the diagnosis of polymyositis. We believe a study of the proteins to be useful not only in diagnosis but for a better understanding of the nature of this disease. In support of this contention we report a group of six cases of proved polymyositis.

Method.—For this electrophoretic study we used Kohn's (1958) cellulose acetate technique, 5 μ l. of serum being applied under current (120 v. constant) on strips 12 by 2.5 cm. for one and a half hours. The barbitone buffer was pH 8.6 and ionic strength 0.05. The protein staining was done with 2 g. of Ponceau S. (G. T. Gurr) in 30 g./1,000 ml. trichloroacetic acid, while the glycoproteins were stained with Feulgen-Schiff, according to Bodman (1957). The quantitative evaluation was done with a reflectance densitometer (Chromoscan). Normal values are shown in Figs. 1 and 2.

Case 1

A 26-year-old West Indian man was admitted to Maida Vale Hospital under the care of Dr. S. Nevin on December 20, 1960, with a history of muscular stiffness and pain of three months' duration, starting in his legs and spreading to his upper limbs.

On examination he showed some generalized muscular wasting, more particularly of the shoulder-girdles and both hands. There was considerable muscle tenderness and weakness, and he was unable to sit up unaided or lift his head from the pillow. The limb-weakness was more proximal than distal, but he had flexure contractures of both elbows and fingers. He also had purulent bronchitis and a generalized lymphadenopathy. A diagnosis of polymyositis was made, and on December 22 the right deltoid muscle was examined with a needle electrode; the findings were those of myositis. A serum electrophoretic strip on

the same day (Fig. 3) revealed a considerable rise in the γ -globulin, followed by a decrease in the albumin fraction; 24 hours previously the E.S.R. had shown only a fall of 4 mm. in one hour (Westergren). Muscle biopsy of the medial head of the triceps on the right side was thought to be consistent with polymyositis.

Six days after admission he was started on prednisone 40 mg. daily, and by March, 1961, it had been reduced to 20 mg. daily. Further serum electrophoretic studies on January 2, 1961, showed changes similar to the initial strip,

FIG. 2. — Normal glycoproteins.

FIG. 1.—Proteins in normal serum.

FIG. 3.—Case 1. Electrophoretic strip. December 22, 1960 (see Table).

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while an E.S.R. on January 6 still showed only a fall of 8 mm. in one hour (Westergren). E.M.G. studies were repeated on January 18, the findings again being thought compatible with polymyositis. He was discharged on May 9 symptomatically much improved though still with considerable motor weakness and on prednisone 10 mg. daily. In August his motor power was greatly improved but he still had some muscular discomfort, and a further serum electrophoretic strip still showed a marked elevation of the γ -globulin fraction with a decrease in the albumin. Thereafter prednisone was maintained at 5 mg. daily.

Case 2

A 54-year-old woman was first admitted to Maida Vale Hospital under the care of the late Dr. E. Blake Pritchard on March 21, 1960, with a complaint of weakness of her legs dating back some seven years. For about a year she had noticed some difficulty in rising from a chair, and during this time had also been troubled by weakness of her arms. Six weeks before admission, when attending hospital on account of a fall, she was found to have bilateral quadriceps wasting. She had no sensory symptoms and no skin changes, but she did admit to occasional difficulty in swallowing solid food.

Examination revealed mild bilateral ptosis with suggestive weakness of the orbicularis oculi, while the upper limbs showed proximal weakness with slight wasting of the shoulder-girdles; in the legs there was considerable proximal wasting and weakness, and also gross weakness of the trunk muscles. Her E.S.R. was 18 mm. in one hour (Westergren).

A muscle biopsy from the right quadriceps muscle on March 31 revealed atrophying muscle but no certain evidence of either a dystrophy or myositis. Results of E.M.G. studies at this time on both quadriceps muscles were thought to be consistent with a primary muscle disorder.

A tentative clinical diagnosis of a late muscular dystrophy was made and she was discharged on April 2. Her condition appeared, if anything, to deteriorate, and she now began to complain of aching muscular discomfort, more particularly in the lower limbs. The possibility of polymyositis was reconsidered and prednisone 20 mg. daily was started in September with slight improvement. A serum electrophoretic strip on November 8 showed a considerable rise in the γ -globulin fraction with a decreased albumin, but an E.S.R. on that date showed only a 4-mm. fall in one hour (Westergren).

On May 15, 1961, she was readmitted and a second muscle biopsy of the left peroneus longus showed undoubted changes of polymyositis. She was discharged on June 10 symptomatically improved on prednisone 15 mg. daily. Since then she has remained in reasonable health.

Case 3

A 63-year-old woman was admitted to Maida Vale Hospital under the care of Dr. Redvers Ironside on February 27, 1959, with a history of weakness of her legs for two years and weakness of her left arm and hand for one year. For some three months prior to admission she had experienced slight difficulty in swallowing solids. She was noted to have acne rosacea with mild bilateral ptosis and facial weakness; there was also proximal muscular wasting and weakness of all four limbs, and she was unable to assume the sitting position from the supine. The deep tendon reflexes were sluggish, the plantars were flexor, and all modalities of sensation were intact. An E.S.R. on March 2 showed a fall of only 9 mm. in one hour (Westergren), but a biopsy of the left biceps on March 5 was thought compatible with polymyositis. A serum electrophoretic paper strip on March 23 revealed a considerable increase in the γ -globulin fraction with a decrease in the albumin. She was started on prednisone 60 mg. daily on March 14, and this medication was continued, though in decreasing dosage, until her discharge on April 11. During this period there was undoubted but limited improvement.

While she was an out-patient her weakness appeared to be helped to a slight degree first by neostigmine and later by pyridostigmine bromide. She was readmitted in July, 1960, because of severe varicose ulcers, and at this time her physical signs were essentially those previously recorded. A further paper electrophoretic strip on April 24, 1961, revealed a similar pattern to that initially found. On January 17, 1962, she showed some increased weakness of her left arm, and a further serum cellulose acetate electrophoretic strip again revealed a considerable increase of the γ -globulin fraction with a reduced albumin; her E.S.R. showed a fall of only 7 mm. in one hour (Westergren). Her condition, however, remitted without further resort to steroid therapy.

Case 4

A man of 61 was admitted to Maida Vale Hospital under the care of Dr. R. A. Henson on August 9, 1955. He had been in excellent health until six weeks prior to this date, when he developed pain in both shoulder-girdles aggravated by movement. Three weeks later he was aware of weakness in his arms associated with some swelling of the arm muscles; in addition he was troubled by dysphagia and painful discomfort of his thigh muscles. He was said to have always had a "high colour," but his wife had observed that his face was unusually red throughout this summer.

On admission he was cyanosed and had an erythematous macular rash over the front of his chest; he also showed some impairment of swallowing and had a "Donald Duck" type of speech. Examination of the motor system revealed a proximal wasting and weakness of the arms and legs, with marked impairment of intercostal movement and weakness of the trunk muscles, while both biceps and forearm muscles were swollen and tender. The deep tendon reflexes were all sluggish, the plantars flexor, and all modalities of sensation intact.

An E.S.R. two days after admission showed only a fall of 1 mm. in one hour, but a serum electrophoretic paper strip four days later revealed a moderate increase of the γ -globulin fraction with a decreased albumin and a slight increase in the α_1 - and α_2 -globulin fractions. Muscle biopsy of the right biceps on August 12 revealed changes of polymyositis. The diagnosis of dermatomyositis had indeed been made on admission, and on the same day he was started on A.C.T.H. gel 100 units daily; nine days later this was replaced by cortisone 50 mg. eight-hourly, but he continued to deteriorate, and died of bronchopneumonia on August 19. Necropsy confirmed the diagnosis of polymyositis.

Case 5

A 63-year-old man was admitted to the West End Hospital for Neurology and Neurosurgery under the care of Dr. Rowland Hill on January 17, 1961, with the complaint of stiffness and aching of his limbs for four months. Examination disclosed swelling, induration, and a reddish-brown pigmentation of the skin of his arms, chest, and neck, and to a less extent of the face and legs. In the upper limbs there was a generalized weakness, more particularly proximally, with evident wasting—in the lower limbs he showed a moderate generalized decrease in power. Movement was also considerably restricted in all the large joints and in the fingers.

On January 18 his E.S.R. showed a fall of 28 mm. in one hour (Westergren), while next day a serum electrophoretic paper strip revealed a considerable increase in the γ -globulin fraction with a decrease of the albumin—the α_1 and α_2 -globulin fractions were at the upper range of normal values. A muscle and skin biopsy from the anterior tibial compartment of one of the lower limbs showed changes consistent with a diagnosis of "scleroderma-dermatomyositis." He was started on prednisone 60 mg. daily on January 18 with some improvement, and later was also given quinine and methandienone; "relaxin" was added later. He made reasonable progress and was discharged home on May 11, on prednisone 10 mg. t.d.s., together with the other added drugs. He was to be followed up at another hospital.

Case 6

In February, 1961, a 55-year-old man developed a "bronchitic illness" from which he recovered only slowly. A month later he became aware of dysphagia and weakness of his limbs, more particularly his arms, while he was seen to have an erythematous rash on his neck and hands which spread rapidly, to become almost generalized. X-ray examination of his chest revealed a large right hilar mass. A diagnosis of a bronchial neoplasm with dermatomyositis was made. Bronchoscopy confirmed the presence of a neoplasm, and radiotherapy was commenced.

On admission to Maida Vale Hospital under the care of Dr. P. H. Sandifer on June 11, 1961, he had a dusky erythema of his face and neck, with similar changes over his hands and a milder generalized erythematous-maculorash. generalized wasting and weakness, proximally greater than distally. The deep tendon reflexes were just obtainable, the plantars flexor, and all modalities of sensation intact. He still had considerable dysphagia.

A serum electrophoretic strip on June 14 (Fig. 4) revealed a great increase of the γ -globulin and a decreased albumin; there was also a marked elevation of the α_2 -globulin and a slight rise of the α_1 -globulin fractions. An E.S.R. on this date showed a fall of 92 mm. in one hour (Westergren). E.M.G. studies of the proximal muscles of the upper limbs carried out a week later showed a pattern consistent with polymyositis, while further serum electrophoretic strips on July 21

FIG. 4.—Case 6. Electrophoretic strip, June.

and August 15 revealed changes similar to the original strip, and an E.S.R. on the latter occasion disclosed a fall of 104 mm. in one hour (Westergren).

He was given large doses of prednisone on admission, starting with 60 mg. daily, and his skin changes and muscular weakness showed some improvement. His general state, however, deteriorated, and in August a subcutaneous nodule appeared over the medial side of his left thigh; a biopsy of the nodule showed anaplastic squamous carcinoma. Later, further secondary deposits appeared over the chest wall, and he died on December 15.

Discussion

In these six cases of polymyositis the notable serum electrophoretic changes were a considerable increase in the γ -globulin fraction and a decrease in the albumin (see Table). Only in Case 3 was the albumin within normal limits; but here the low normal α_1 -, α_2 -, and β -globulin fractions should be noted. In Case 4 the γ -globulin was not as grossly elevated as in the other five, but it should be emphasized that this strip was taken two days before death: this was the only patient with a low total protein, the level in the other five being within normal limits. Although such a serum electrophoretic pattern may be found in other pathological conditions its presence in a patient with muscle disease would seem to be highly suggestive of polymyositis.

Only in Case 6 (Fig. 4) were the α -globulin fractions clearly elevated—the α_2 fraction to a considerable degree and the α_1 fraction only slightly—and this was the

	Total Protein g./100 ml.	Absolute Values				
		Alb.	Globulins			
			α_1	α_2	β	γ
Average normal (28)	6-80	4-00	0-28	0-66	0-80	1-08
Normal range (28)	6-0-8-0	3-25-4-84	0-10-0-43	0-41-0-91	0-60-0-94	0-74-1-34
Case 1 ..	6-47	2-67	0-21	0-68	0-80	2-11
" 2 ..	7-58	2-78	0-29	0-82	1-07	2-62
" 3 ..	7-28	4-39	0-05	0-42	0-69	1-73
" 4 ..	5-50	1-84	0-39	0-87	0-99	1-41
" 5 ..	7-88	3-28	0-41	0-82	1-05	2-32
" 6 ..	6-20	2-00	0-51	0-38	0-59	1-72

patient with dermatomyositis and a proved underlying bronchial neoplasm. In the other two patients with skin involvement the α -globulin fractions, though tending to be higher than in the cases of polymyositis alone, remained essentially at the upper range of normal values. It was of some interest that only in Case 6, with the raised α_2 -globulin fraction, was the E.S.R. grossly elevated, with falls of 92 and 104 mm. in one hour (Westergren); in the other two patients with skin changes it was mildly elevated in the one and normal in the other; and in the remaining two patients it was normal with the exception of an isolated reading of a fall of 18 mm. in one hour (Westergren) in Case 2.

In two patients we estimated the glycoproteins. In Case 1 (Fig. 5), a patient with polymyositis alone, the strip revealed only a slight increase in the γ -glycoprotein, while in Case 6 (Fig. 6), with an underlying neoplasm, it faithfully reflected the increase in the α_2 -globulin fraction and exaggerated the slightly raised α_1 -globulin fraction on the protein strip. In such a way does a glycoprotein strip emphasize tissue-destruction, and it is of interest that such changes were found in a patient with an underlying bronchial neoplasm. It might be that such a glycoprotein trace in a case of polymyositis should lead one to suspect the possibility of an underlying neoplasm.

Both Walker and Benditt (1950) and van Sande (1954) stressed the consistent finding of a considerably elevated γ -globulin fraction and a decreased albumin in patients with polymyositis; however, van Sande found the α_2 -globulin fraction consistently raised in his five patients, while Walker and Benditt reported a considerable decrease in the total protein in their four cases. With one exception—and this an electrophoretic strip taken two days before death—we found the total protein in all our patients to be within normal limits, while in only one instance was the α_2 -globulin elevated; this was in

FIG. 5.—Case 1. Glycoproteins.

FIG. 6.—Case 6. Glycoproteins.

the patient with an underlying bronchial carcinoma, and, we would suggest, was probably a reflection of the underlying condition.

The impressive increase of the γ -globulins in these patients sets several problems. Is this increase the cause or the direct or indirect consequence of the polymyositis? Is it that the increased γ -globulin reflects a reaction of the organism against a pathogenic agent, or are there autoantibodies?

It would be of interest to know if any immunological reaction could be elicited between this abnormally increased γ -globulin and products prepared from fresh surgical material such as an amputation. This, together with more extended studies on this subject, we propose to pursue.

Summary

The essential and striking electrophoretic changes in six patients with proved polymyositis were a markedly elevated γ -globulin fraction followed by a decreased albumin; such a pattern, while not of course specific for this condition, would, we feel, be highly suggestive of polymyositis in a patient with muscle disease.

The α_2 -globulin fraction was raised only in the one patient who had both dermatomyositis and an underlying bronchial neoplasm. In the other two patients with skin involvement it remained at the upper limit of normal.

The E.S.R. was strikingly raised only in the patient with the underlying neoplasm—in the remaining two cases with skin involvement it was normal in the one and slightly raised in the other. In the remaining three patients with polymyositis alone it was consistently normal with a single isolated exception, when the fall was only 18 mm. in one hour (Westergren).

The glycoproteins were estimated in two patients, revealing an increased γ -glycoprotein fraction in the one with polymyositis alone and showing a tissue-destruction pattern in the patient with an underlying bronchial neoplasm.

We would like to thank Dr. W. H. McMenemey for his advice and encouragement and the various members of the consultant staff of Maida Vale Hospital for allowing us access to their patients. We are also grateful to Dr. Rowland Hill for permission to include a patient under his care at the West End Hospital. We are further indebted to Dr. McMenemey and Dr. H. C. Grant for the pathological reports and to Dr. H. R. Townsend for the E.M.G. studies.

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"Presiding at a prize-giving ceremony [on October 24] at the Middlesex Hospital School of Nursing, Lord Astor of Hever expressed regret that he had to give up the chairmanship of the hospital because he is to live in the south of France. The matron, Miss Marjorie J. Marriott, expressed appreciation of his work for the hospital. He had been a member of the board for 40 years and chairman since 1938. His weekly visits to the hospital had been greatly appreciated by patients and staff. When he was appointed chairman there were 380 nurses, compared with 890 at present, and the hospital had 450 beds, compared with nearly 1,000 now." (*The Times*, October 25.)

RHEUMATOID PERICARDITIS

A REPORT OF FOUR CASES

BY

MATTHEW WILKINSON, M.D., M.R.C.P.

From the Royal Northern and Charing Cross Hospitals, London

As in other collagen diseases, an increasing incidence and variety of systemic lesions are being recognized in rheumatoid arthritis. These include cardiac lesions, which have been shown to be frequent in most necropsy studies (Baggenstoss and Rosenberg, 1941; Fingerma and Andrus, 1943; Young and Schwedel, 1944; Bauer and Clark, 1948). By contrast, clinical studies have demonstrated heart lesions rather infrequently during life (see review by Rogen, 1947).

After excluding conditions common in elderly subjects, such as ischaemic and hypertensive heart disease, the following cardiac lesions have been reported from post-mortem studies on rheumatoid arthritic subjects.

1. Macroscopic sclerosis of valve cusps and chordae tendineae with microscopical inflammatory and degenerative changes in valve cusps and myocardium. These are similar to the lesions of rheumatic heart disease and have been found in from 6% (Bennett, 1943) to 66% (Young and Schwedel, 1944) of necropsies on rheumatoid subjects. The clinical recognition of rheumatic heart disease is very much less frequent even in patients subsequently found to have cardiac lesions at necropsy (Baggenstoss and Rosenberg, 1941, Young and Schwedel, 1944). Whether these lesions represent an undue disposition to rheumatic heart disease among rheumatoid subjects or whether they are part of the rheumatoid disease process remains uncertain.

2. Rheumatoid granulomata, histologically similar to the subcutaneous nodules of rheumatoid arthritis, have been reported in the pericardium, myocardium, valve cusps, and aorta. Such lesions are infrequent and probably affect only 1 to 3% of patients (Sokoloff, 1953).

3. Rheumatoid aortitis with aortic-valve incompetence is more commonly seen with ankylosing spondylitis, but 2 of the 22 cases reviewed by Clark *et al.* (1957) and one described by Hope-Ross *et al.* (1960) suffered from peripheral arthritis only.

4. Pericarditis or adhesions have been reported in from 11% (Fingerma and Andrus, 1943) to 50% (Young and Schwedel, 1944) of patients dying with rheumatoid arthritis. Here again clinical recognition lags far behind the pathological incidence.

The following four cases of rheumatoid pericarditis represent the only cases diagnosed in a series of 197 rheumatoid patients admitted to the Charing Cross and Royal Northern Hospitals between January, 1956, and March, 1962. Two of the four patients were seen personally and the other two are described from their case records.

Case 1

The patient, a man aged 48, was admitted to hospital in February, 1962. In 1956, after a period of kneeling to lay a concrete path, he developed painful swollen knees, followed by pain and stiffness of other joints. His arthritis was controlled with prednisolone, chloroquine, and salicylates, but for six months prior to admission he had received no corticosteroids. Three days before admission he awakened with moderately severe anterior chest pain and dyspnoea, but continued his work in spite of discomfort until an exacerbation on the morning of admission. There was no exacerbation of his arthritis. For several years he had suffered from mild bronchitis.