DIGESTIVE AND ARTICULAR MANIFESTATIONS OF COLLAGEN DISEASES

A STUDY OF 55 PATIENTS

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It is common to find both articular and digestive manifestations accompanying certain disorders of connective tissue. Impressed by the frequency of those manifestations we decided to study a group of 55 patients suffering from systemic lupus erythematosus, scleroderma, dermatomyositis, and polyarteritis nodosa.

Systemic Lupus Erythematosus (S.L.E.).—This is a systemic disease of connective tissue running an irregular and generally severe course. 91 per cent. of cases described by Shearn and Pirofsky (1952) were females, and a similar incidence (90·5 per cent.) was found in the present group. The articular manifestations of S.L.E. are very frequent, may appear at any stage of the disease, and may precede lesions of skin and viscera by a period of months or years. Tumulty and Harvey (1949) found that in seventeen of their 32 patients the disease began with stiffness or arthralgia. In some cases the articular manifestations presented as an acute migratory polyarthritis resembling that of rheumatic fever; when this type of arthritis preceded the skin lesions the real diagnosis of S.L.E. was often missed. In other cases the arthritis was chronic and progressive resembling rheumatoid arthritis (R.A.) (Ross and Wells, 1953). Both large and small joints may be involved, occasionally resulting in permanent deformity, but the more usual pattern is one of mild and transient arthritis which can be readily differentiated from primary articular disease.

We studied 21 patients with S.L.E. (Table I), all of whom had joint involvement, nine having gastrointestinal symptoms as well. These nine patients with both arthritic and digestive symptoms were of special interest to us and have been analysed in detail. Joint involvement either preceded the systemic disease by a period of time which varied

from 1 month to 5 years, or appeared simultaneously with the skin rash. Seven cases started with arthritis, two with arthralgia; arthritis was present in the ankles (3 cases), knees, wrists, proximal interphalangeal (P.I.P.) joints, and elbow (1 case each); arthralgia occurred in the elbow and costo-sternal joints (1 case each). As the disease progressed other joints became involved. Arthritis was most frequently observed in the ankles, P.I.P. joints, knees, elbows, and wrists; arthralgia in elbows, lumbar and cervical spine, and the temporo-mandibular joints (Table II). In this series the arthritis was usually milder than that seen in R.A. and improved with corticosteroid therapy. Intra-articular effusion was rarely observed in cases of S.L.E. by Ropes and Bauer (1953), but Houli (1958) found effusion in three out of sixteen cases. The synovial fluid was pale yellow and turbid and did not usually form a clot; mucin was type G (precipitation with acetic acid). In two of these three patients the cellular content of the synovial fluid was 40-80 R.B.C. per c. mm., leucocytes 100-200/c. mm. (lymphocytes 75-90, monocytes 10-80, granulocytes 0-12).

Alimentary disturbances are frequently found in S.L.E. Anorexia, nausea, vomiting, intestinal cramps, diarrhoea, and abdominal pains (which may simulate biliary colic or acute appendicitis) are the commonest symptoms (Dubois, 1952). Gomes (1952) found alimentary symptoms in 30 per cent. of ten patients, nausea and vomiting being most prominent. Tumulty and Harvey (1949) observed severe diarrhoea in five out of 32 patients and reported hepatomegaly due to "fat infiltration" as common. These alimentary manifestations merely indicate that the usual lesions of the disease (*viz.* necrotizing angiitis and intimal and elastic proliferation) have become localized in the digestive tract in the same way that arterial and other collagen

TABLE I
DISTRIBUTION OF ARTICULAR AND DIGESTIVE MANIFESTATIONS IN 55 PATIENTS WITH COLLAGEN DISEASES

Disease	Number of Cases	Manifestations							
		Articular Only		Digestive Only		Both Articular and Digestive		No Articular or Digestive	
		No.	per cent.	No.	per cent.	No.	per cent.	No.	per cent.
Systemic Lupus Erythematosus	21	12	57.1	0	—	9	42.8	0	—
Scleroderma	20	7	35.0	0	—	10	50.0	3	15.0
Dermatomyositis	11	7	63.6	0	—	4	36.3	0	—
Polyarteritis	3	1	33.3	1	33.3	1	33.3	0	—
Total	55	27	49.0	1	1.8	24	43.6	3	5.4

lesions are found in the kidneys, spleen, liver, and other organs of the body. The digestive symptoms may precede, appear simultaneously with, or follow other symptoms. In all our nine patients the digestive upsets appeared after joint involvement; they are detailed in Table III, which illustrates the non-specificity of these symptoms. In addition one patient had both an intestinal haemorrhage and perforation. Severe abdominal cramp, possibly caused by lesions in the peritoneum, mimicked biliary colic and appendicitis in two cases. Lesions of the liver are of serious import and histological examination

showed the presence of fatty degeneration and necrosis of the liver cells, interstitial mononuclear infiltration, and fragmentation of the trabeculae. Clinically, the symptoms are those of mild hepatitis—the so-called “lupus hepatitis”—*i.e.* hepatomegaly, jaundice, and alteration in the plasma proteins, especially in the gamma globulin fraction. Three in the present series had lupus hepatitis. One patient exhibited the disease in its more chronic form—“lupoid hepatitis”—which occurs predominantly in females and is characterized by protracted abdominal discomfort, jaundice, fever, abnormal

TABLE II
DISTRIBUTION OF JOINT INVOLVEMENT IN 24 PATIENTS WITH DIGESTIVE AND ARTICULAR MANIFESTATIONS

Joints	Disease								Total
	Systemic Lupus Erythematosus		Scleroderma		Dermatomyositis		Polyarteritis Nodosa		
	A	B	A	B	A	B	A	B	
Knees	5	2	3	4	2	1	—	—	17
Ankles	7	2	2	3	1	1	1	—	17
P. I. Phalangeals	6	2	5	2	—	—	—	—	15
Elbows	3	5	—	2	—	—	—	—	10
Lumbar Spine	—	4	—	2	—	3	—	1	10
Cervical Spine	—	4	—	3	—	2	—	—	9
Temporo-Mandibular	—	3	—	3	—	—	—	—	6
Metacarpo-Phalangeals ..	1	—	3	—	—	—	1	—	5
Wrists	3	—	1	1	—	—	—	—	5
Sacral Spine	—	—	—	—	—	2	—	—	2
Shoulders	—	2	—	2	—	1	—	—	5
Hips	—	1	—	—	—	—	—	—	1
Dorsal Spine	—	—	—	—	—	1	—	—	1
Costo-Sternal	—	1	—	—	—	—	—	—	1
Total	25	26	14	22	3	11	2	1	104

A = Arthropathy.
B = Arthralgia.

TABLE III
DISTRIBUTION OF DIGESTIVE MANIFESTATIONS IN 24 PATIENTS WITH COLLAGEN DISEASES
WITH ARTICULAR AND DIGESTIVE TROUBLES

Digestive Manifestations	Disease							
	Systemic Lupus Erythematosus		Scleroderma		Dermatomyositis		Polyarteritis Nodosa	
	No.	per cent.	No.	per cent.	No.	per cent.	No.	per cent.
Anorexia	6	66·6	5	50·0	2	50·0	1	100
Diarrhoea	4	44·4	3	30·0	0	—	1	100
Cramp	3	33·3	0	—	2	50·0	1	100
Full Stomach	3	33·3	0	—	2	50·0	0	—
Odynophagia	3	33·3	3	30·0	1	25·0	0	—
Hepatomegaly	3	33·3	2	20·0	1	25·0	0	—
Vomiting	2	22·2	5	50·0	2	50·0	1	100
Nausea	2	22·2	4	40·0	2	50·0	1	100
Constipation	2	22·2	5	50·0	0	—	0	—
Dysphagia	1	11·1	7	70·0	0	—	0	—
Total No. of Cases ..	9		10		4		1	

liver function tests in association with arthralgia, a positive L.E. cell test, presence of circulating auto-antibodies, skin rash, hypergamma-globulinaemia, and severe systemic disturbance. Fortunately, lupoid hepatitis improves with corticosteroid therapy. It must be remembered, however, that arthritic manifestations are a commoner accompaniment of S.L.E. than disorders of the alimentary canal (Table I).

Scleroderma.—This is a systemic disorder of connective tissue that occurs most frequently in middle-aged women; it involves the skin and subcutaneous tissue predominantly and various viscera to a lesser degree. In each of our twenty cases the diagnosis was confirmed by skin biopsy. Ten patients had both alimentary and articular symptoms and are described in detail; seven had articular involvement alone and three had skin lesions alone (Table I).

The articular symptoms in the ten patients with both articular and alimentary lesions were either mono- or poly-articular, and both arthritis (4 cases) and arthralgia (6 cases) were observed. In eight of these patients the arthritic symptoms preceded the onset of digestive disturbances and in two the order was reversed. Arthritis initially involved the P.I.P. and knee joints, but other joints were affected at a later stage of the disease. Arthralgia was more common than arthritis (Table II). Five patients developed deformities during the evolution of the disease: claw-hand in three, absorption of the finger nails in one, and ankylosis of one wrist in one.

Whenever the articular symptoms preceded the skin lesions they were misdiagnosed as R.A. despite negative agglutination tests.

These ten patients presented a variety of digestive upsets (Table III). Lesions were most frequently found in the oesophagus, followed by the small bowel, colon, and stomach. Oesophageal lesions occurred in 70 per cent. of our patients and initial dysphagia became progressively worse, culminating in vomiting. Radiographically, the first sign was cessation of peristalsis in the lower third of the oesophagus followed by dilatation and finally rigid sclerosis. The upper two-thirds of the oesophagus were either normal or dilated. The cardia may remain open allowing regurgitation and stagnation of food, oesophagitis, and finally ulceration.

Lesions in the small bowel are most frequent in the duodenum and proximal part of the jejunum (Villamil and Mancini, 1959) and the symptoms consist of meteorism, peri-umbilical pain, nausea, and vomiting. Areas of decreased motility and dilatation are seen on radiographs. Colonic involvement produces constipation (50 per cent. of cases) or diarrhoea (30 per cent. of cases) and radiologically dilated loops with loss of tonus may be seen. Sometimes the x-ray pictures resemble those of chronic ulcerative colitis. Gastric symptoms were difficult to define. Hepatomegaly occurred in 20 per cent. of our patients.

Dermatomyositis.—This is a general disease of connective and muscular tissue involving the skin and skeletal muscles and resulting in marked muscular atrophy and contractures.

In our group of eleven patients with dermatomyositis four had both arthritic and alimentary manifestations (Table I). In these four cases arthralgia occurred more frequently than arthritis, and stiffness was thought to be due to fibrositis of neighbouring muscles and not to actual joint lesions. Both arthritis and arthralgia predominantly affected the knees, lumbar spine, and ankles (Table II).

Involvement of the gastro-intestinal tract is believed to be due to lesions in smooth muscle and results in nausea, vomiting, gastric fullness, and cramps (Table III). One patient had hepatomegaly; microscopy revealed interstitial hepatitis and proliferation of Kupffer cells as identified by Stoia (1962).

Polyarteritis Nodosa.—This is a disease of the connective tissue of blood vessels characterized by perivascular inflammatory nodes associated with focal fibrinoid necrosis of the intimal layer of medium and small vessels. The disease occurs most frequently in males between the ages of 20 and 40, but may also occur in childhood (Adelson, 1951; Dent, Strange, Sako, and York, 1953; Fager, Bigler, and Simonds, 1951).

The final picture of the disease is pleomorphic; lesions can occur in any part of the body and the resulting symptoms are correspondingly varied. We studied three patients, all males. One had articular involvement, the second digestive symptoms, and the third presented both. In this third patient digestive symptoms appeared 60 days after the onset of arthritis (Tables I, II, and III). One of our patients died and necropsy showed chronic oesophagitis and generalized visceral ischaemia.

Other authors with larger series of patients have described the gastro-intestinal manifestations in detail. Nuzum and Nuzum (1954) found alimentary involvement in 62 per cent. of 175 cases, and Mowrey and Lundberg (1954) in 45 per cent. of 607 cases. Abdominal pain, nausea, and vomiting were the commonest symptoms, and small bowel lesions resulted in diarrhoea (Lawrie, 1955), intestinal obstruction (Lowenstein and Heeb, 1955), small bowel infarction (Rabinovitch and Rabinovitch, 1954), intraperitoneal haemorrhage and gastro-intestinal perforation (Lovell and Rose, 1955). If the liver is involved the clinical picture is that of hepatitis and the pathological lesions of cirrhosis of Laënnec's type may be seen. Pancreatic involvement is shown by acute haemorrhagic infarction or by chronic interstitial pancreatitis.

Summary

A group of 55 patients was studied with connective tissue disorders—systemic lupus erythematosus,

scleroderma, dermatomyositis, and polyarteritis nodosa. 51 of these patients had joint involvement and 25 had digestive disturbances. The 24 patients presenting with both arthritic and alimentary symptoms were studied in detail. Nine had systemic lupus erythematosus and in each of these the articular symptoms preceded the alimentary disturbances by a period of months or years. In eight of the ten patients with scleroderma arthritic symptoms preceded gastro-intestinal disease. Four cases of dermatomyositis and one of polyarteritis nodosa are also described. The large joints were involved more frequently than the small ones and arthralgia was more common than arthritis. The alimentary symptoms were very varied. The distribution of both arthritic and alimentary symptoms is described in detail.

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Manifestations digestives et articulaires des maladies du collagène. Etude de 55 malades**RÉSUMÉ**

On étudia un groupe de 55 malades souffrant de désordres du tissu conjonctif—lupus érythémateux disséminé, sclérodermie, dermatomyosite et polyartérite noueuse. L'atteinte articulaire fut trouvée chez 51 d'entre eux et des troubles digestifs chez 25 d'entre eux et des troubles digestifs chez 25 d'entre eux. On étudia minutieusement les 24 malades qui combinaient les symptômes arthritiques et alimentaires. Neuf d'entre eux souffraient de lupus érythémateux disséminé et chez tous les neuf les symptômes articulaires avaient précédé les troubles alimentaires de mois ou d'années. Chez 8 sur 10 malades atteints de sclérodermie, les symptômes arthritiques avaient précédé la maladie gastro-intestinale. On décrit aussi 4 cas de dermatomyosite et un de polyartérite noueuse. Les grandes articulations étaient impliquées plus souvent que les petites et l'arthralgia était plus habituelle que l'arthrite. Les symptômes alimentaires étaient très variés. On décrit minutieusement la distribution des symptômes arthritiques et alimentaires.

Manifestaciones digestivas y articulares en las enfermedades del colágeno. Estudio de 55 enfermos**SUMARIO**

Se estudio un grupo de 55 enfermos con disturbios del tejido conectivo—lupus eritematoso diseminado, esclerodermia, dermatomiositis y poliarteritis nodosa. La afección articular fué encontrada en 51 de ellos y disturbios digestivos en 25. Se investigaron detalladamente los 24 enfermos que manifestaron síntomas tanto artríticos como alimenticios. Nueve de estos padecían de lupus eritematoso diseminado y en todos ellos los síntomas articulares habían precedido los disturbios alimenticios de meses o de años. En 8 de los 10 enfermos con esclerodermia, los síntomas artríticos habían precedido la enfermedad gastrointestinal. Se describen cuatro casos de dermatomiositis y uno de poliarteritis nodosa. Las grandes articulaciones se veían implicadas con más frecuencia que las pequeñas y artralgia fué más común que artritis. Los síntomas alimenticios fueron muy variados. Se describe detalladamente la distribución de los síntomas artríticos y alimenticios.