tightness aggravated by deep respiration as well as pain in ankles and knees. Physical examination showed a pericardial friction rub and polyarthritis affecting ankles and knees. The electrocardiogram showed widespread elevation of ST segments and chest x ray examination an increase in heart size compatible with pericardial effusion. Laboratory tests showed haemoglobin 73 g/l, packed cell volume 0.22, reticulocytes 3%, platelets $119 \times 10^9/l$, and white blood cell count $3.78 \times 10^9/l$ (56% neutrophils, 1% eosinophils, 2% basophils, 34% lymphocytes, 6% monocytes, 1% myelocytes). Erythrocyte sedimentation rate was 118 mm/h. Blood and urine chemistries were within normal limits. A thick smear for malaria was negative. The Coombs direct test (polyspecific anti-globulin, anti-IgG, anti-C3b/C3d) was negative and Coombs indirect test was also negative. Antinuclear antibody test was positive at a titre of 1/800 (speckled pattern), dsDNA antibodies (Farr's technique) were not detected, and complement levels were normal. Cardiolipin antibodies (enzyme linked immunosorbent assay (ELISA)) were detected (IgG isotype at high level and IgM at moderate level) and lupus anticoagulant was negative. Tissue antibodies were present (antiparietal cells 1/100, antismooth muscle 1/200). Antinuclear cytoplasmic and histone antibodies were negative. Circulating immune complexes were 76 $\mu g/ml$. The same day, treatment with quinine was withdrawn with a prompt relief of symptoms within 24–48 hours and laboratory tests returned to normal within two weeks. After a one year follow up the patient remains asymptomatic and no autoantibodies are detected in her serum.

Multiple quinine dependent antibodies have been reported as being responsible for a variety of clinical syndromes associated with anaemia, leucopenia, thrombocytopenia, coagulopathies, renal failure, and disseminated intravascular coagulation.^{8,9} However, a lupus-like syndrome and production of cardiolipin antibodies induced by this drug have not been previously described. Interestingly, histone antibodies, which are often found in other drug induced lupus-like syndromes, were not detected in our patient. On the other hand, although malaria itself may produce a number of immunological abnormalities—including the production of cardiolipin antibodies,¹⁰ it is unlikely that this infection was the cause of the lupus-like syndrome and the cardiolipin antibodies because these appeared when the patient was afebrile and with a thick smear negative for *Plasmodium falciparum*, and disappeared after withdrawal of quinine.

Quinine should be considered as the potential cause when patients receiving this drug present with either a lupus-like syndrome or with signs of a coagulation disorder. Failure to consider quinine as a possible cause for the symptoms will lead to delay in diagnosis and prolonged morbidity, whereas both syndromes will disappear quickly when quinine treatment is stopped.

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Scleroderma and the watermelon stomach

The watermelon stomach is an unusual cause of gastrointestinal blood loss and iron deficiency anaemia. We report on two patients who presented with the watermelon stomach and subsequently developed typical features of scleroderma.

A previously healthy 72 year old white woman was found to have a haemoglobin of

62 g/l. Colonoscopic evaluation disclosed non-bleeding rectal arteriovenous malformations. A small bowel series was unremarkable. Oesophagogastroduodenoscopy showed parallel hyperaemic longitudinal rugal folds (stripes) across the gastric antrum with intervening normal appearing mucosa consistent with the watermelon stomach. Nd:YAG laser coagulation treatment was given, with resolution of blood loss. Over the next six months she developed Raynaud's phenomenon, arthritis, and sclerodactyly.

A diagnosis of limited scleroderma was made and over the next several months her arthritis and Raynaud's phenomenon improved and she had no progression in skin thickening. Five months after the diagnosis of limited scleroderma she developed melena and her haemoglobin dropped to 70 g/l. At that time the scleroderma was otherwise quiescent. Oesophagogastroduodenoscopy again showed vascular lesions consistent with watermelon stomach and she was treated with Nd:YAG laser coagulation, with resolution of the bleeding.

A 40 year old African American man with a history of hypertension and hypothyroidism presented with fatigue and swelling of his hands. Laboratory evaluation showed a haemoglobin of 116 g/l (previous haemoglobin 159 g/l). Colonoscopy showed small haemorrhoids. Oesophagogastroduodenoscopy showed linear erythematous streaking of the antrum consistent with a watermelon stomach (figure).

Eight months after the onset of his illness, physical examination showed tendon friction rubs and diffuse skin thickening, and he was diagnosed with diffuse scleroderma. Gastric antral vascular ectasia, or the watermelon stomach, so called because of its distinctive endoscopic appearance which resembles the stripes of a watermelon, is a rare cause of chronic gastrointestinal bleeding. Endoscopically, longitudinal rugal folds are seen traversing the antrum and converging on the pylorus.¹ Histopathologically, ectatic mucosal blood vessels with capillary thrombi characterise watermelon stomach.²

The watermelon stomach has been reported to occur in association with autoimmune diseases.¹ Patients with gastric antral vascular ectasia and scleroderma have been

Watermelon antrum with erythema (patient No 2).

rarely described.³⁻⁹ Hypothyroidism, as was present in our second patient, has also been described in association with watermelon stomach.¹⁰

Our patients represent cases in which gastrointestinal bleeding secondary to the watermelon stomach was an early manifestation of their scleroderma. Similarly, Rosekrans, *et al* described one patient in whom anaemia secondary to bleeding from the watermelon stomach predated the diagnosis of scleroderma.⁴ Most cases of watermelon stomach, however, have been reported to occur in those who already have well established scleroderma.^{3,9}

Bleeding from the watermelon stomach and activity of scleroderma did not necessarily parallel each other. In the first case recurrent bleeding from the watermelon stomach occurred when other manifestations of scleroderma were quiescent. In the second case the manifestations of the watermelon stomach and the activity of the scleroderma progressed concurrently. Progression of scleroderma and concomitant bleeding from the watermelon stomach have been reported,⁵ but it is not known whether this is always the case. Further cases will need to be examined to determine the relation between the activity of the watermelon stomach and progression of the scleroderma.

Doctors should be aware that watermelon stomach may be an early manifestation of scleroderma, and bleeding from the watermelon stomach may occur any time during the course of disease.

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Improvement of severe pulmonary hypertension in a patient with SLE

The development of pulmonary hypertension during the course of connective tissue diseases is associated with a grim prognosis^{1,2} as no treatment has shown sustained efficacy. Heart-lung transplantation may be undertaken, but experience in patients with systemic disease is limited, costly, and disappointing.^{1,2} We report on a patient with advanced pulmonary hypertension arising in the course of systemic lupus erythematosus (SLE) successfully treated with vasodilator and immunosuppressive drugs.

In 1990 SLE was diagnosed in a 22 year old white woman who presented arthralgias, myalgias, pericarditis, Raynaud's phenomenon, hypocomplementaemia, high titre anti-nuclear antibodies with speckled pattern (anti-Sm, anti-RNP) without DNA or phospholipid antibodies. Low dose prednisone (10 mg/d) was started. Exertional dyspnoea, syncope and signs of right side heart insufficiency appeared in January 1991, related to precapillary (pulmonary capillary wedge pressure 7 mmHg) pulmonary hypertension (table). Neither thromboembolism—that is, normal pulmonary angiography, nor interstitial lung disease were present. Heart-lung transplantation was considered, but not performed because no donors were available at that time.

In January 1992 corticosteroid treatment (500 mg pulse methylprednisolone for three days, followed by oral prednisone 0.5 mg/kg/d) in combination with monthly pulse cyclophosphamide (750 mg) and mesna were instituted. After two months a dramatic haemodynamic (table) and clinical improvement was observed: the patient had significant resolution of her dyspnoea and was able to walk. Thus in January 1993 prednisone was tapered and pulse cyclophosphamide was given once every three months. At that time the patient returned to work. In September 1994, when the patient had received a total of 20 cyclophosphamide courses over a period of 32 months without any side effects, she decided to stop intravenous treatment, and only low dose prednisone with prazosin was continued. She chose to stop prazosin in July 1995. The last haemodynamic investigation performed in September 1995 (table) showed an improvement in pulmonary hypertension with both an increase in cardiac index (+73%) and a decrease in mean pulmonary artery pressure (–44%).

Our patient had several of the variables associated with poor survival rates in patients with pulmonary hypertension³: New York Heart Association functional class IV, presence of Raynaud's phenomenon, raised mean pulmonary arterial pressure, decreased cardiac index. Immunosuppressive treatment—cyclophosphamide infusions once a month for 12 months followed by quarterly infusions, in combination with steroid treatment—resulted in prolonged decrease of pulmonary pressure together with dramatic clinical improvement. Improvement might have resulted from treatment with high dose steroids or cyclophosphamide, or both, and could not be attributable to cyclophosphamide only. The association of vasodilator with immunosuppressive drug treatment might have been helpful, even though the initial treatment with vasodilator alone was ineffective. A few cases of improvement with immunosuppressive drug treatment have been reported. Corticosteroids alone are rarely efficient. An initial but not sustained response to high dose methylprednisolone has been reported in a patient with mixed connective tissue disease.⁴ Goupille *et al*⁵ reported the case of a lupus patient with precapillary pulmonary hypertension who was successfully treated with high doses of corticosteroids, with an appreciable follow up of 18 months.⁵ A woman with mixed connective tissue disease and pulmonary hypertension improved after sequential administration of cyclophosphamide and cyclosporin A over a period of 10 years.⁴ Groen *et al* described a prolonged—but only partial—improvement with low dose prednisone and quarterly cyclophosphamide infusions in a woman with SLE and pulmonary hypertension.⁶

In conclusion, the prolonged and excellent outcome seen in our patient supports treatment with immunosuppressive drugs associated with vasodilator agent in precapillary pulmonary hypertension arising in SLE, before considering heart-lung transplantation. Controlled trials of immunosuppressive drug treatment in patients with SLE and precapillary pulmonary hypertension are needed.

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Evolution of haemodynamic findings before (January 91 and 92) and after two (March 92), 14 (June 93), and 20 (September 95) cyclophosphamide infusions

Treatment	PAP* (mmHg)	Mean PAP (mmHg)	PVR* (mmHg/l/min/m ²)	CI* (l/min/m ²)	Pao ₂ (mmHg)
Normal values	19 (5)/8 (3)	10-20	<5	3-3.5	80-100
January 91 Prednisone 5 mg/d	94/41	57	26	2.2	60
January 92 + prazosin 5 mg/d Prednisone 30 mg/d	85/40	55	ND	ND	60
March 92† + monthly cyclophosphamide Prednisone 30 mg/d	66/27	36	ND	ND	78
June 93 + monthly cyclophosphamide Prednisone 15 mg/d	78/28	48	13.7	3.5	82
September 95 + quarterly cyclophosphamide (stopped in September 94) Prednisone 5 mg/d	54/18	32	8.5	3.8	96

*PAP = pulmonary artery pressure, systolic/diastolic; PVR = pulmonary vascular resistance; CI = cardiac index; Pao₂ = arterial O₂ tension, breathing room air.

†PAP calculated with echocardiography.