was noted with low doses of prednisone, however, in contrast with the dramatic improvement obtained in the original papers.6 7 On the other hand, synovial biopsy in our case did not show malignant infiltration. Thus it is reasonable to suggest that the rheumatic manifestations belong to a paraneoplastic syndrome, as has been previously reported with other neoplasms.8 9 To our knowledge this is the first description of peripheral synovitis and pitting oedema as an initial manifestation of non-Hodgkin’s lymphoma. We would like to emphasise the need to consider the possibility of an underlying malignancy in a patient with these clinical characteristics who is unresponsive to the usual medical treatment.

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Angiogenins converting enzyme in rheumatoid arthritis

Sir: Being interested in vascular endothelial cell transdifferentiation,1 I read with interest the instructive articles by Veale et al2 and Goto et al3 about the angiogenins converting enzyme production in rheumatoid arthritis. Although there is no doubt that vascular endothelial cells participate in this process, the role of macrophages remains questionable because the antibodies used for their identification (antiCD14) are not macrophage specific and cross react with vascular endothelial cells.4 5 Moreover, undifferentiated vascular endothelial cells can transdifferentiate into macrophage-like cells and migrate into the extravascular space.6 It may be useful to re-evaluate the role of macrophages in rheumatoid arthritis in the light of the new knowledge about the transdifferentiation of vascular endothelium.7 For example, the mesenchymal transformation cells responsible for joint destruction differentiate into fibroblasts in due course and are not, therefore, inflammatory cells. McCachren considers, however, any collagenase producing cells immunoreactive with Leu-M3 or HAM56 to be macrophages.8 Again, these antibodies are not macrophage specific and cross react with vascular endothelium.9 10 Mesenchymal transformation cells found in undifferentiated vascular endothelial cells1 by their character and aggressiveness.7 The facts that antiangiogenis suppresses arthritis11 and that angiogenins II is an angiogenic factor12 are in excellent keeping with that proposition.

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Endothelium damage and von Willebrand factor antigen

Sir: We read with great interest the recent paper by Blann et al1 on damage to the endothelium in Sjögren’s syndrome.2 The authors examined the relation of the autoantibodies SSA and SSB to endothelium damage using serum levels of von Willebrand factor antigen (vWFAg) as an index of damage to the endothelium. Damage of the endothelium may be present in Sjögren’s syndrome, but there is no real evidence whether such damage results in high or low levels of vWFAg. The extent of production of vWFAg in megaekayocytes in Sjögren’s syndrome and other diseases is unknown; mainly because of the complexity of the factor do not follow changes in the numbers of thrombocytes in peripheral blood and so this production site is no longer a part of the scenario. Further, in our opinion, endothelium damage cannot explain why increased concentrations of vWFAg are present in such varied diseases as proliferative glomerulonephritis, diabetes mellitus, systemic scleroderma, Sjögren’s syndrome, and arteritis temporalis, as endothelial damage in these diseases is not a common denominator.

We have recently studied the immunohistochemistry in arteritis temporals, in which
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AUTHOR'S REPLY: Elling et al propose that raised circulating levels of von Willebrand factor antigen (vWFAg) reflect not endothelial cell damage but production by endothelial cells in newly growing microvasculature, challenging existing dogma.1,2 In support of this hypothesis they offer an immunohistological photograph from a patient with temporal arteritis taken from a previous publication which examined temporal artery biopsy specimens from patients with arteritis temporalis, polymyalgia rheumatica, and other disease.3 They found raised serum vWFAg and intense vWFAg staining in new vessels in the lamina elastica only in patients with arteritis temporalis, but offer no mechanism or evidence that these are 'new' vessels. Could it be that the intense staining seen in the elastic lamina is because these endothelial cells are damaged? From the photograph it is difficult to tell if all or part of the intense staining for vWFAg is from intact cells, disrupted cells, or from vWFAg in the general connective tissue stroma.

I am surprised that Elling et al suggest that endothelial damage cannot explain why increased concentrations of vWFAg are present in such varied diseases as proliferative glomerulonephritis, diabetes mellitus, systemic sclerosis, Sjögren's syndrome, and arteritis temporalis, as endothelial damage in these diseases is not a common denominator.4 Other workers, such as Compi et al, have expressed an opposite view, stating that vessel injury is a common feature of scleroderma, glomerulonephritis, diabetes mellitus, Behçet's syndrome, systemic lupus erythematosus, rheumatoid arthritis, and vasculitis in general.5 There seems to be little disagreement about the presence of raised vWFAg in a large number of conditions, some of which may be characterised by histological evidence of injury to the vasculature. However, the exact mechanism, in many cases, is unclear. Raised vWFAg is common in the acute phase response,6 but it would be surprising if there was evidence of damaged endothelium in this condition. It may be that in this case endothelial cells are merely 'activated' or 'stimulated' to produce vWFAg in expectation of a more severe insult (i.e. septis), but they indeed damage the endothelium. Further increases in vWFAg may be the product of increased synthesis by actively growing cells in the capillary beds, the adventitia, elsewhere. If this were true then one would need to explain why there should be an extra growth of endothelial cells, or upregulated production from a resting cell. Perhaps existing cells are being damaged, possibly to the point of cell death, by a disease process, such as the combined effects of immune complexes and complement in vasculitis6 or ketoacidosis in diabetes.7

Probably the ultimate proof of injury/damage would be an electron micrograph study of the endothelium in human disease. Such work would need to show a damaged endothelial cell with absent or depleted Willebrand bodies (storage granules of vWFAg), ideally with immunocytochemistry for cytoplasmic vWFAg, alongside plasma levels of vWFAg. Another approach may be to look at vWFAg mRNA from in vivo 'damaged' and 'normal' endothelial cells—but these data would not provide information about vWFAg in Willebrand bodies.

Until such data are easily obtained then the hypothesis that raised vWFAg is produced by injured endothelial cells in vivo may never be completely accepted. Yet despite this there remains a wealth of clinical and non-clinical data from many different diseases which all support the hypothesis. Convincing competing hypotheses would need to take account of all these findings.

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