

## LYMPHSPIRATION

## FACTOR VIII AND NEOPLASTIC ENDOTHELIUM

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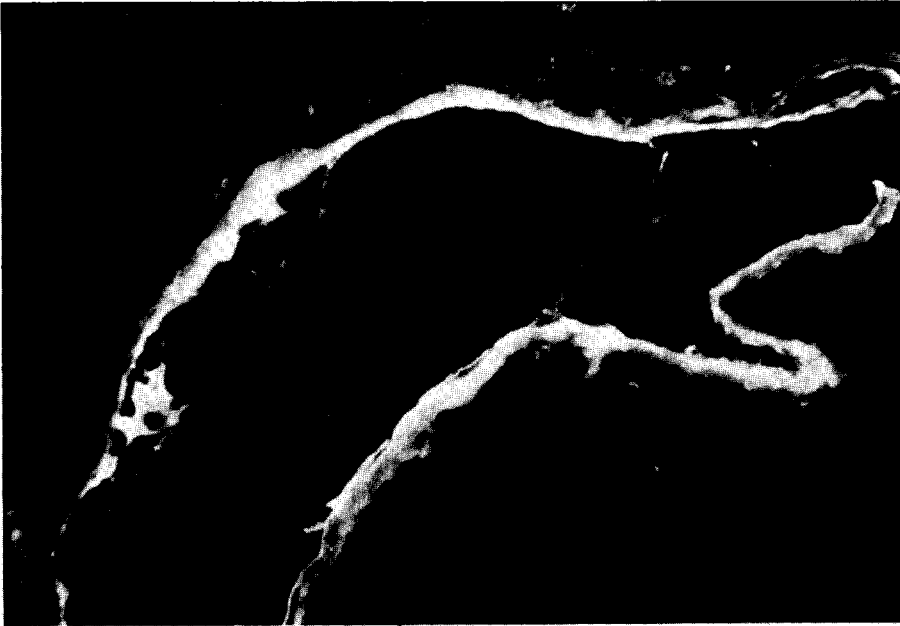
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Integral to Dorfman's postulate of a lymphatic origin for Kaposi's sarcoma are the staining characteristics of vascular endothelium for factor VIII-associated antigen (see Lymphspiration—Histogenesis of Kaposi's Sarcoma—this issue). Whereas blood vascular endothelium reacts strongly to factor VIII monoclonal antibody (immunoperoxidase and immunofluorescence), lymphatic endothelium has been reported as negative in some studies (1,2). Gnepp (3), on the other hand, claims that tissue cultures of canine lymphatic endothelium do react positively for factor VIII-associated antigen. Moreover, we have now examined intact canine lymphatics and large visceral lymphogenous cysts in man and each demonstrates, both on snap-frozen and paraffin sections as well as tissue culture of lymphangiomatous endothelium, factor VIII-associated antigenicity (Fig. 1).

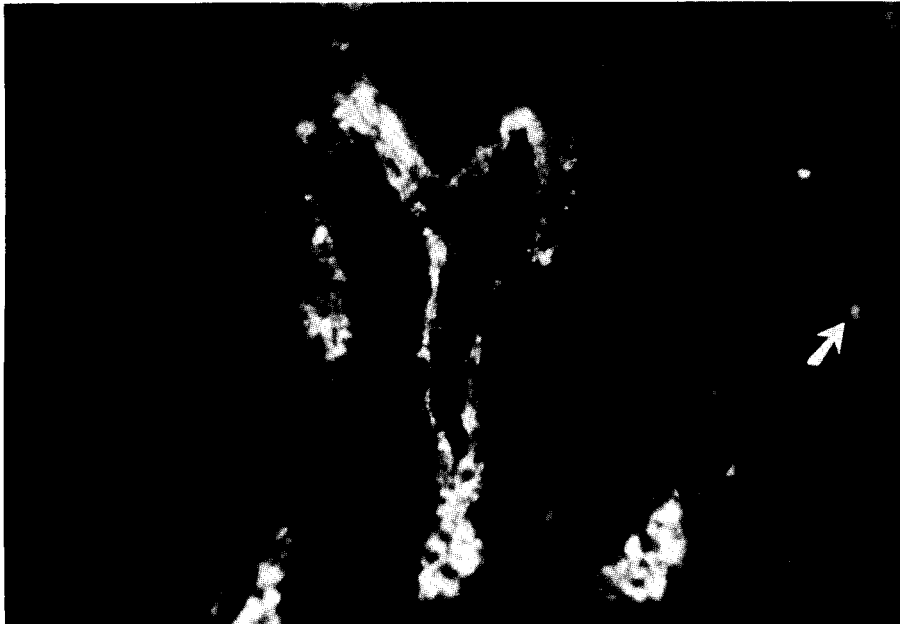
It is ironic that Stewart-Treves "lymphangiosarcoma" that arises in lymphadenomatous limbs and has long been considered of lymphatic origin is now reclassified as "angiosarcoma" based on positive reactivity of tumor cells to factor VIII-related antigen (4). Conversely, Kaposi's sarcoma which has long been considered an "angiosarcoma" is now proposed to be of lymphatic origin by Dorfman in part because of his observation of non-reactivity for factor VIII-associated antigen in his series of Kaposi's sarcoma. This last contention is in doubt, however, as most

investigators ((5-8) have identified factor VIII-associated antigen in at least the endothelial element of Kaposi's sarcoma; some reports indicate negative results in the spindle cell population of Kaposi's (7,8). We include a photomicrograph of a case from our institution of Kaposi's sarcoma demonstrating strong factor VIII-associated antigen positivity by direct immunofluorescence (Fig. 2). Possible explanations for divergent findings by the immunohistochemical approach include differences in antigen preservation resulting from differing fixation and tissue processing techniques (7), failure to employ appropriate controls, and variability in antibody specificity, particularly when commercial antisera are employed (9).

There is a body of information, however, that suggests the diversity of findings relates to differences in differentiation or antigen expression of vascular endothelium in pathologic states. First, blood vascular endothelium in Von Willebrand's disease apparently loses its capacity to manufacture factor VIII, a key element in the bleeding diathesis (10). Second, the intensity of factor VIII-associated antigen positivity in Kaposi's sarcoma has been reported to vary from patient to patient and among various areas within a given tumor, even when performed by an experienced laboratory using the same techniques and the same antisera (6). Finally, poorly differentiated vascular neoplasms



*Fig. 1: Strong positivity for factor VIII-associated antigen of endothelial cells lining large lymphangiomatous spaces (FITC-conjugated anti-factor VIII-associated antigen, 2275x).*



*Fig. 2: Kaposi's sarcoma showing intense positivity for factor VIII-associated antigen within endothelial cells. Note only rare positive cells in spindle-cell stroma (arrow) (FITC-conjugated anti-factor VIII-associated antigen, 1420x).*

such as angiosarcoma and some benign vascular neoplasms (e.g. cellular hemangioma) fail to demonstrate factor VIII-associated antigen positivity (11,12). Such problems in confirming the endothelial nature of neoplasms may be solved in part by the use of a second endothelial marker such as *Ulex europaeus* lectin, which reacts with the less well-differentiated areas of angiosarcomas (13).

Dorfman's Lymphspiration is "mind-stretching" particularly in light of the infectious nature of acquired immunodeficiency syndrome (AIDS) with prominent lymphologic antecedents and manifestations. Perhaps, however, the absence of a single antigen marker (i.e., factor VIII) merely signifies that synthetic capability in neoplastic endothelium is diminished or lost due to retro-differentiation as a manifestation of oncogenesis.

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