OEDEMA

IS IT ALL FLUID?

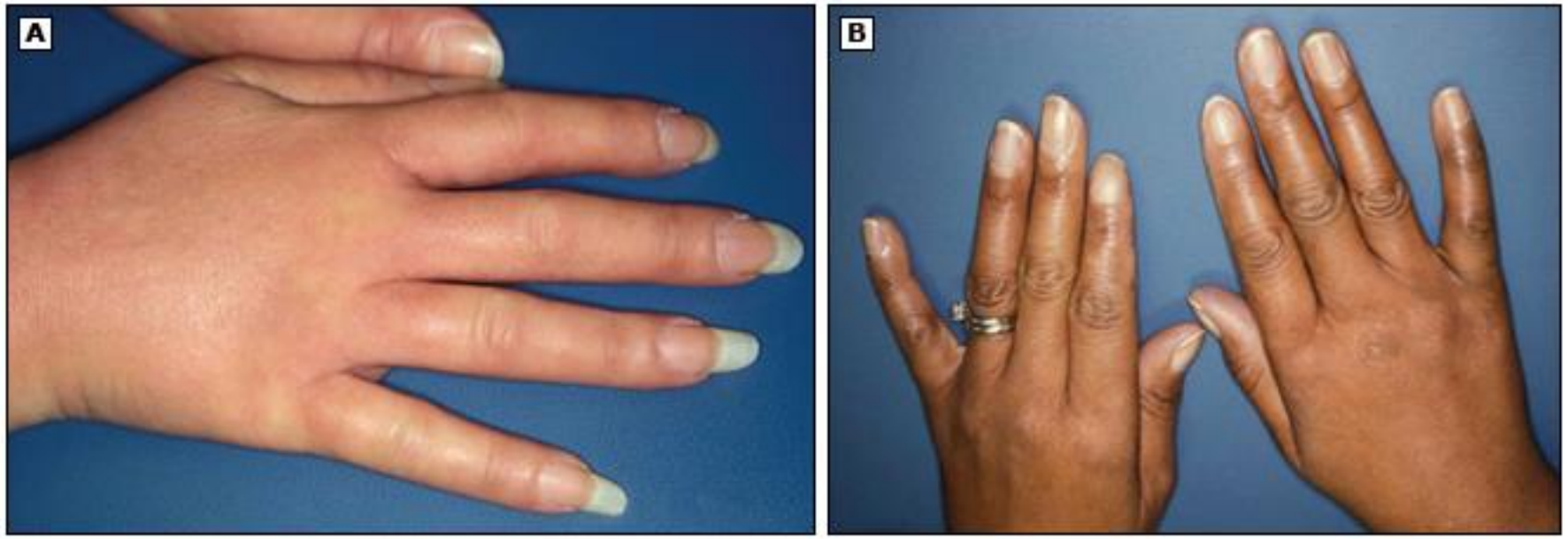
DON’T FORGET THE CELLS

How Oedema and Swelling Present to the Rheumatologist

- Clinical Presentations
  - Inflammatory arthritis
    - Rheumatoid Arthritis
    - Polymyalgia Rheumatica
    - Crystal Arthritis
      - Gout
      - CPPD arthritis
    - Psoriatic Arthritis
  - RS3PE (Remitting Seronegative Symmetrical Synovitis with Pitting Oedema)
  - CRPS (Complex Regional Pain Syndrome) aka Reflex Sympathetic Dystrophy
  - Scleroderma
    - Acute early stage/later recurrence
    - Multiorgan involvement Cardiac/Respiratory/Renal
- Oedema as a diagnostic clue.
- Oedema as an alarm bell.

- Insights and Questions

Puffy hands and shiny skin in early systemic sclerosis



(A) Diffusely puffy fingers are a common initial presentation.

(B) Shiny skin suggests impending skin thickening.

Hand swelling and edema in PMR

Swelling and pitting edema of the hand developing early in the course of PMR in an 84-year-old woman. The patient's other hand was similarly swollen. Swelling resolved with glucocorticoid therapy.

PMR: polymyalgia rheumatica.

Courtesy of Gene Hunder, MD.

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Remitting seronegative symmetrical synovitis with pitting edema

An 80-year-old man with the acute onset of pain and swelling at the hands. Symptoms and signs responded briskly to prednisone 10 mg in the morning and 5 mg at night.

Reproduced from: Docken WP. Polymyalgia rheumatica and giant cell arteritis. In: Targeted Treatment of the Rheumatic Diseases, Weisman MH, Weinblatt ME, Louie JS, Van Vollenhoven RF (Eds), Elsevier, 2010. p. 186.

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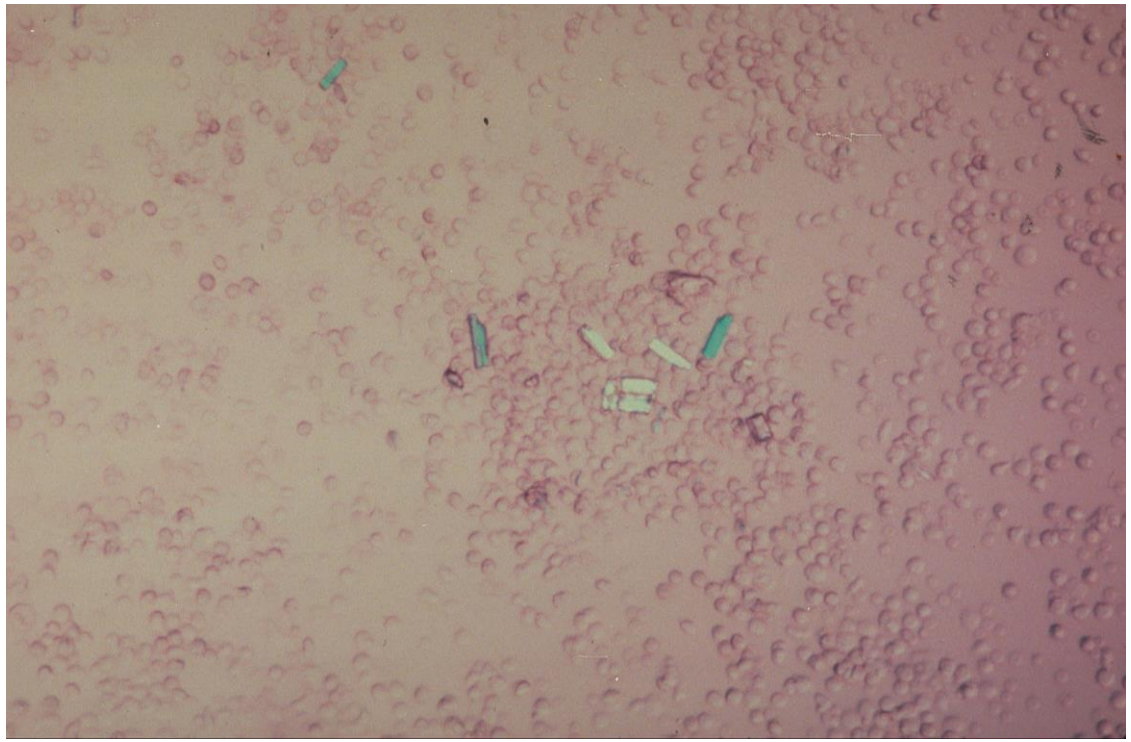
Acute Inflammatory Arthritis

Rheumatoid arthritis
Acute Viral Polyarthritis
Ross River
Parvo
Barmah Forest
SLE
Other CTD

Psoriatic Arthritis



Acute Crystal Arthritis

Typical CPPD crystals in aspirate

Complex Regional Pain Syndrome

Generalized Oedema in CTD Patients

Scleroderma/SLE/RA

- The development of prominent lower limb or generalized oedema in patients with CTD is a **Red Flag**.
    - **Internal organ involvement that may contribute to generalized oedema**

        Cardiac

        Renal

        Respiratory

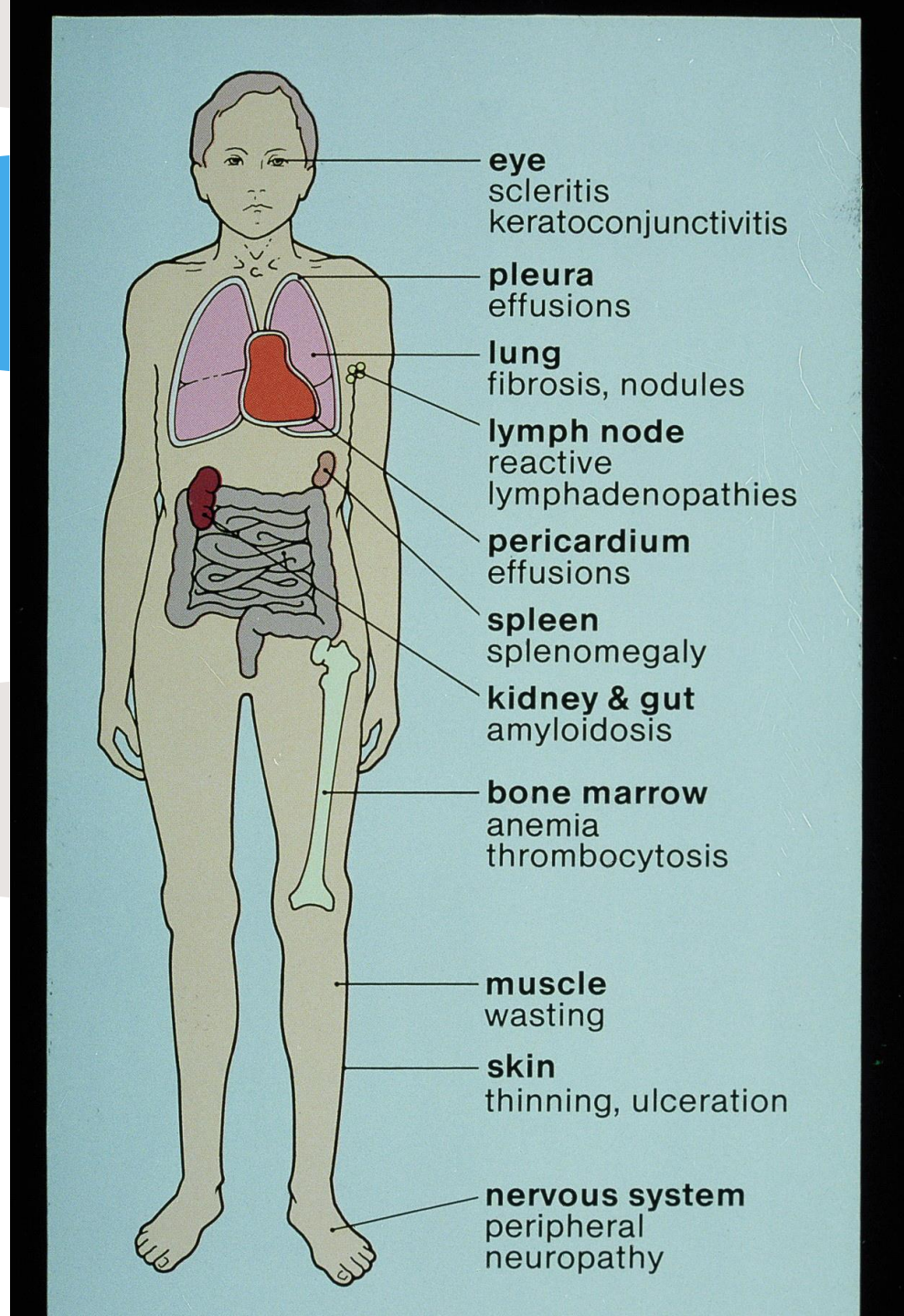
        Hepatic

    Prompt aggressive treatment may be required to arrest progression of organ damaging and potentially fatal disease.

Multi-Organ Involvement in Connective Tissue Disease

- This old diagram shows the extent of possible organ involvement in uncontrolled Rheumatoid Arthritis.

- Current RA treatments have effectively prevented many of these problems but other CTDs can still develop them.



Clinical features of the major systemic sclerosis subsets

Diffuse cutaneous	Early (<3 years after onset)	Late (>3 years after onset)
Constitutional	Fatigue and weight loss	Minimal, weight gain typical
Vascular	Raynaud often relatively mild	Raynaud more severe, more telangiectasia
Cutaneous	Rapid progression involving arms, trunk, face	Stable or regression
Musculoskeletal	Prominent arthralgia, stiffness, myalgia, muscle weakness, tendon friction rubs	Flexion contractures and deformities, joint/muscle symptoms less prominent
Gastrointestinal	Dysphagia, heartburn	More pronounced symptoms, midgut and anorectal complications more common
Cardiopulmonary	Maximum risk for myocarditis, pericardial effusion, interstitial pulmonary fibrosis	Reduced risk of new involvement but progression of existing established visceral fibrosis
Renal	Maximum risk for renal crisis within the first 5 years	Renal crisis less frequent, uncommon after 5 years
Limited cutaneous	**Early (<10 years after onset)**	**Late (>10 years after onset)**

Insights and Questions

- Localized swelling is a frequent finding in inflammatory CTD.
  - Treatment of the inflammation usually settles the swelling.
  - More prominent swelling with pitting oedema does occur and also frequently responds to treatment.
- Generalized oedema may be a signal of severe internal organ involvement and requires prompt assessment and management.
- The swelling/oedema is contributed to by increased fluid and the actions of activated inflammatory and immune cells that are present.
- **What Role do Lymphatics Play?**

Lymphatic Function in Autoimmune Diseases

- *Noa Schwartz 1,2, Madhavi Latha S. Chalasani 1, Thomas M. Li 1, Zhonghui Feng1,*
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Lymphatic vessels are critical for clearing fluid and inflammatory cells from inflamed tissues and also have roles in immune tolerance. Given the functional association of the lymphatics with the immune system, lymphatic dysfunction may contribute to the pathophysiology of rheumatic autoimmune diseases. Here we review the current understanding of the role of lymphatics in the autoimmune diseases rheumatoid arthritis, scleroderma, lupus, and dermatomyositis and consider the possibility that manual therapies such as massage and acupuncture may be useful in improving lymphatic function in autoimmune diseases.

Conclusions and Future Directions

- The lymphatic system has not been well-studied in autoimmune diseases generally, but the existing evidence, especially in RA and, to a more limited extent, in systemic sclerosis suggests that there is at least dysfunction of lymphatic flow.

- Further studies focused on the consequences of dysfunctional flow as well as alterations in the direct effects of lymphatic vessels and LECs on innate and adaptive immune cells should provide insights into how best to target the lymphatics in autoimmune rheumatic diseases.

- Additionally, understanding the causes of lymphatic dysfunction in these diseases may help us better target upstream mediators and perhaps reveal that lymphatic targeting is a mechanism of action of some medications.

- **Finally, as we consider new approaches to targeting lymphatics in autoimmune diseases, there may be value in better understanding older approaches in the context of Twenty-First century biomedical understanding of lymphatic and immune function to expand our therapeutic armamentarium for autoimmune diseases.**

Manual lymph drainage improving upper extremity edema and hand function in patients with systemic sclerosis in edematous phase

Susanna Maddali Bongi[1], Angela Del Rosso, Mauro Passalacqua, Sara Miccio, Marco Matucci Cerinic

Arthritis Care Research 2011 Aug;63(8):1134-41

- **Objective:** In systemic sclerosis (SSc; scleroderma) patients in edematous phase, hand edema is often present. Manual lymph drainage (MLD) stimulates the lymphatic system and reduces edema. Our aim was to evaluate the efficacy of MLD in reducing edema and in improving functionality of the hands and perceived quality of life (QOL) in SSc patients in edematous phase.
- **Methods:** Of 35 SSc patients with edematous hands, 20 were treated with MLD according to the Vodder technique once a week for 5 weeks (intervention group), and 15 served as the observation group. Patients were evaluated at enrollment, at the end of treatment (T1), and after 9 weeks of followup (T2) by volumetric test (assessing hand volume), the Hand Mobility in Scleroderma (HAMIS) test, and 4 visual analog scales (VAS; scored 0-10) evaluating the perception of hand edema and pain and their interference on daily activities. QOL and disability were assessed by the physical synthetic index (PSI) and mental synthetic index (MSI) of the Short Form 36 (SF-36) and by the Health Assessment Questionnaire (HAQ).
- **Results:** In the intervention group, hand volume, the HAMIS test, and the 4 VAS were improved significantly at the end of treatment ($P < 0.001$). The results were maintained at T2 ($P < 0.001$). The HAQ and the PSI and MSI of the SF-36 also improved significantly at T1 ($P < 0.001$), but only PSI improvement was maintained at T2 ($P < 0.001$). In the observation group, no improvement at T1 and at T2 was observed.
- **Conclusion: In SSc, MLD significantly reduces hand edema and improves hand function and perceived QOL.**

Prolonged Thoracic Duct Drainage in Rheumatoid Arthritis and Systemic Lupus Erythematosus

Diversion of Thoracic-Duct Lymphocytes

Decreased Synovitis in rheumatoid arthritis

Decreased Rheumatoid nodules in rheumatoid arthritis

Decreased Cutaneous vasculitis in systemic lupus erythematosus

Decreased Serum IgG

West J Med. 1979 Apr; 130(4): 309–324.

H E Paulus, H I Machleder, P J Clements, K Nyman, and S Levine

Clinical Case Conference , Dept of Medicine, UCLA School of Medicine.

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OR THE LYMPHATICS !