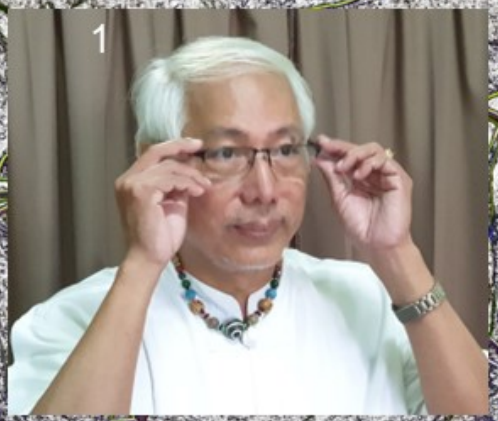


Updates on Rheumatology 2025

UCTD

မသေမချာလေးဖက်နာ

Unclassified Connective Tissue Disease (UCTD)
မသေမချာလေးဖက်နာ

Prof. Chit Soe

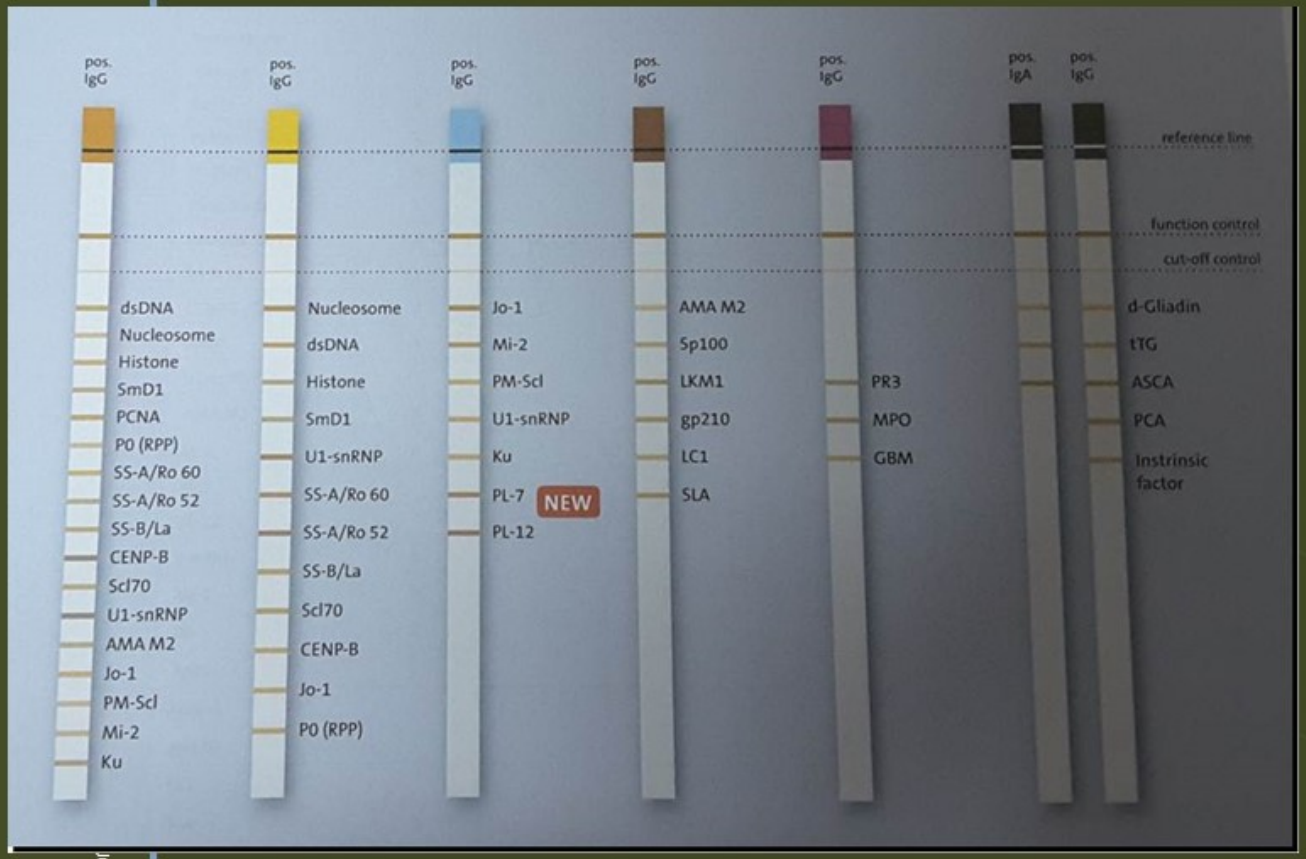
Pre-test

- Can we diagnose someone with ANA positive and no feature of CTD as UCTD?
- Can UCTD cause accumulated organ damage in long-term?
- Can UCTD evolve to classical CTD in long-term?
- Can we prevent UCTD not to change to CTD?
- Is there any role of NSAID in UCTD?
- Is there any role of DMARDs in UCTD?
- Any special care need for Pregnancy?

Diagnosis

- Autoantibody positive for two times
- Not fulfilling the diagnostic criteria of any CTD such as SLE or PSS or RA
- Symptoms persists for more than 6 months

ENA, LIA to see whether ANA+ is due to dsDNA or SM



Vague features of CTD, but not fit to one disease

- arthralgia can be present in up to 86% of patients;
- various skin lesions, including livedo, purpura, acrocyanosis, telangiectasias, and urticaria, can also be common (37%).
- Other common symptoms include the Raynaud phenomenon (33%), sicca symptoms (30%), mucocutaneous symptoms, such as oral ulcers (23%), and arthritis (22%), fever (15%)

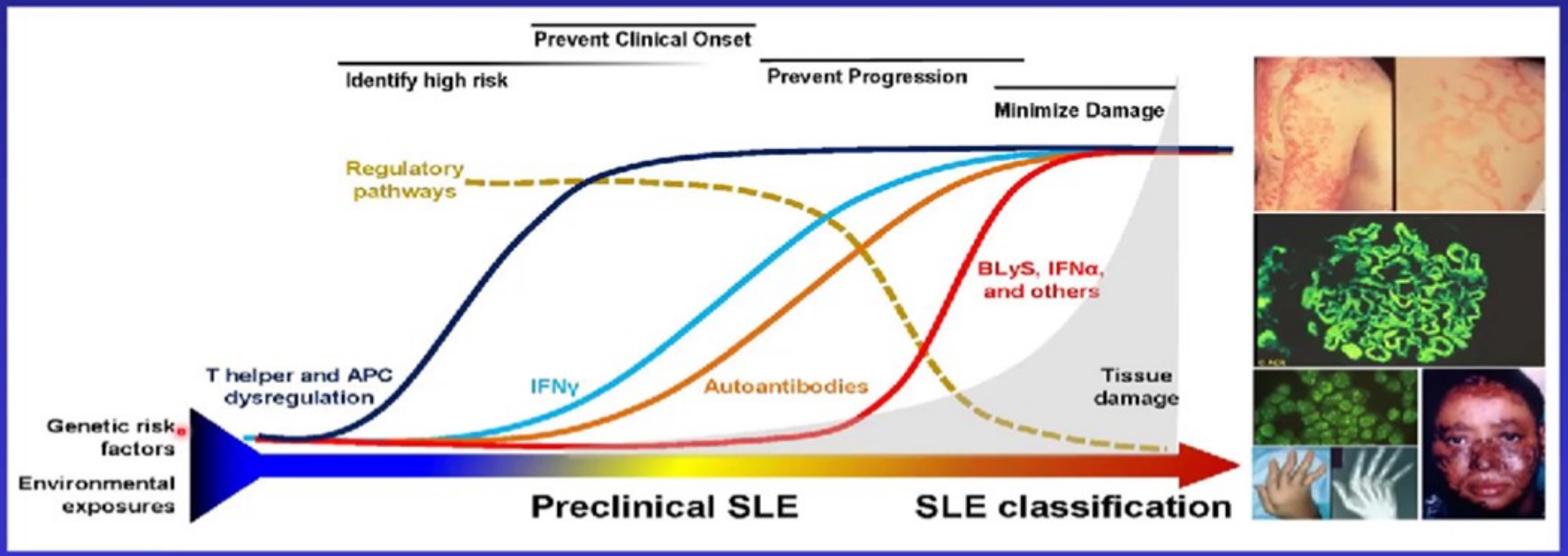
Can we diagnose someone with ANA positive and no feature of CTD as UCTD?

- No
- Undifferentiated connective tissue disease is a clinical entity defined as serological and clinical manifestations of systemic autoimmune disease, however, not fulfilling any criteria of defined connective tissue disease.
- This disease is considered a diagnosis of exclusion
- Up to 90% of the cases are females between 32 and 44 years old

Why?

- Gene + Trigger
- Like other rheumatic diseases, UCTD is not contagious.
- Examples of Triggers include exposure to harmful chemicals, like those found in cigarette smoke, pollutants in the air, ultraviolet light and viruses

Transitioning from Health to SLE



ANA+ asymptomatic; ANA + one or two minor symptom; ANA+ well defined symptoms

Adapted from Harley JB, James JA. Bull NYU Hosp Jt Dis 2006;64:45-50.

- In old time, patient present with CVA or heart failure and diagnose associated HT or DM
- Now, HT or DM was diagnosed fur before CVA or heart failure because of the awareness and screening
- Auto-antibodies appear fur before well-defined CTD, but previously only when patient presented with rash or arthritis or renal failure, ANA or RF are searched
- Now, Auto-antibodies are added in screening program and UCTD becomes common

Can UCTCD cause damage like SLE?

Connective tissue diseases

RMD Open
Rheumatic & Musculoskeletal Diseases

ORIGINAL RESEARCH

Disease evolution and organ damage accrual in patients with stable UCTD: a long-term monocentric inception cohort

Chiara Tani ,[1] Francesca Trentin,[2] Alice Parma,[3] Dina Zucchi ,[4,5] Chiara Cardelli ,[1,6] Chiara Stagnaro,[7] Elena Elefante ,[8] Viola Signorini,[7] Linda Carli,[9] Maria Laura Manca,[1,10] Marta Mosca[10]

To cite: Tani C, Trentin F, Parma A, *et al*. Disease evolution and organ damage accrual in patients with stable UCTD: a long-term monocentric inception cohort. *RMD Open* 2024;**10**:e003967. doi:10.1136/rmdopen-2023-003967

ABSTRACT

Objectives Undifferentiated connective tissue diseases (UCTDs) are systemic autoimmune conditions that cannot be diagnosed nor classified as defined CTD; the majority maintains an undifferentiated profile (stable UCTD, sUCTD) over time. Data on long-term outcomes of sUCTD are lacking.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Undifferentiated connective tissue diseases (UCTDs) are systemic autoimmune conditions that cannot be diagnosed nor classified as defined CTD; the majority maintains an undifferentiated profile (stable UCTD, sUCTD) over time. Data on long-term outcomes of sUCTD are lacking.

- Although less significantly impacted than in patients with SLE,
- in the long- term UCTDs can accumulate organ damage and evolve into defined connective tissue diseases

Accumulated organ damage in SLE (pink) and UCTD (Blue) patients over 20 years

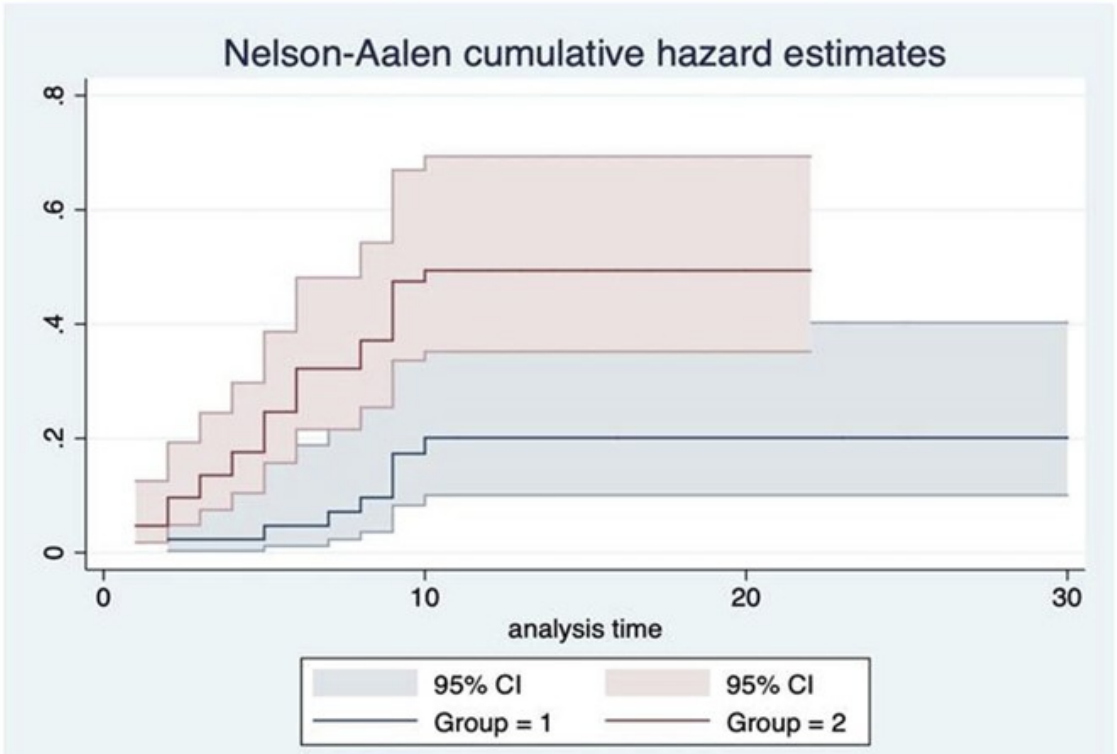


Figure 2 Nelson-Aalen cumulative hazard estimates. Group 1=UCTD; group 2=SLE. SLE, systemic lupus erythematosus; UCTD, undifferentiated connective tissue disease.

Can we prevent damage caused by UCTD?

- The protective role of antimalarials against damage accrual is well established in SLE but some evidence of their usefulness also in UCTD has already been indirectly identified in animal models some years ago

Tani C, *et al. RMD Open* 2024;**10**:e003967. doi:10.1136/rmdopen-2023-003967

CAN UCTD EVOLVE TO CLASSICAL CTD LATER?

Risk of progression to CTD (1/3)

- the risk of progression to a well-defined connective tissue disease is relatively low, especially for those who have remained stable for five years or more
- about 30% of patients with UCTD have an evolving course, with the majority developing SLE or RA within 5-6 years of the UCTD diagnosis

. 2003 May-Jun;21(3):313-20.
. 2003 May-Jun;21(3):313-20.

Five-year follow-up of 665 Hungarian patients with undifferentiated connective tissue disease (UCTD)

- 230 of the 665 true UCTD patients (34.5%) developed a defined CTD,
- (28 systemic lupus erythematosus [SLE], 26 mixed connective tissue disease [MCTD], 19 progressive systemic sclerosis [PSS], 45 Sjögren's syndrome, 3 polymyositis/dermatomyositis [PM/DM], 87 rheumatoid arthritis [RA], and 22 systemic vasculitis.
- 435 of 665 patients (65.4%) remained in the UCTD state, and
- 82 of 665 patients (12.3%) achieved complete remission with symptoms not reappearing within the 5-year period.
- The highest probability of evolution to a defined CTD was during the first 2 years after onset:

High risk for progression

- associated with an increased risk of developing defined connective tissue disease, including having
- high levels of ANA or other antibodies in the blood,
- low blood cell counts, and
- having abnormalities of the small blood vessels in the nailbeds (which are called nailfold capillaries and can be evaluated by a rheumatologist using a special microscope, called a dermatoscope

High Risks found in a Systematic Review

- The predictors for progression to SLE with the highest certainty of evidence included those with
- younger age (MD -5.96 [-11.05-0.87 years]),
- serositis (RR 2.69 [1.61-4.51]), or
- the presence of anti-dsDNA antibodies (RR 4.27 [1.92-9.51]).
- For SSc, the highest certainty of evidence included puffy fingers (RR [3.09 [1.48-6.43]), abnormal nailfold changes (NFC) (avascular areas [RR 5.71 (3.03-10.8)] or active or late SSc pattern [RR 2.24 (1.25-4.01)] and
- anti-topoisomerase-I (RR 1.83 [1.45-2.30]).

Predictors of staying as UCTD for long-term (1/3)

- Anti-Ro/SSA and anti-U1-RNP positive UCTD patients
- Those not progress within 2 years of Dx

Can we prevent UCTD changing to CTD?

Prevention of developing full-blown diseases

- It is unknown whether a particular therapy might decrease the risk of disease flare or of evolution to a defined connective tissue disease.
- Some data suggest that treatment with hydroxychloroquine may decrease the risk or delay possible progression of UCTD to lupus, but this has not yet been confirmed
- Furthermore, vitamin D deficiency can result in pathological changes in the function and number of the CD4+ T-helper cells in patients with undifferentiated connective tissue disease, and the supplementation of vitamin D showed an improvement in the balance of anti-inflammatory and pro-inflammatory processes in the disease.

HCQ in UCTD:

AMERICAN COLLEGE of RHEUMATOLOGY
Empowering Rheumatology Professionals

MEETINGS • KEYWORD INDEX • ADVANCED SEARCH • YOUR FAVORITES • ACR MEETINGS

ABSTRACT NUMBER: 2595

The Role of Hydroxychloroquine in the Treatment of Undifferentiated Connective Tissue Disease

Hayley Epstein[1], Diana P. Pena[2], Bianca Di Cocco[1], Teja Kapoor[3] and Anca Askanase[4], [1]Rheumatology, CUMC, New York, NY, [2]Rheumatology, Universidad Militar Nueva Granada, Bogotá, Colombia, [3]Rheumatology, Columbia University College of Physicians & Surgeons, New York, NY, [4]Rheumatology, Columbia University Medical Center, New York, NY

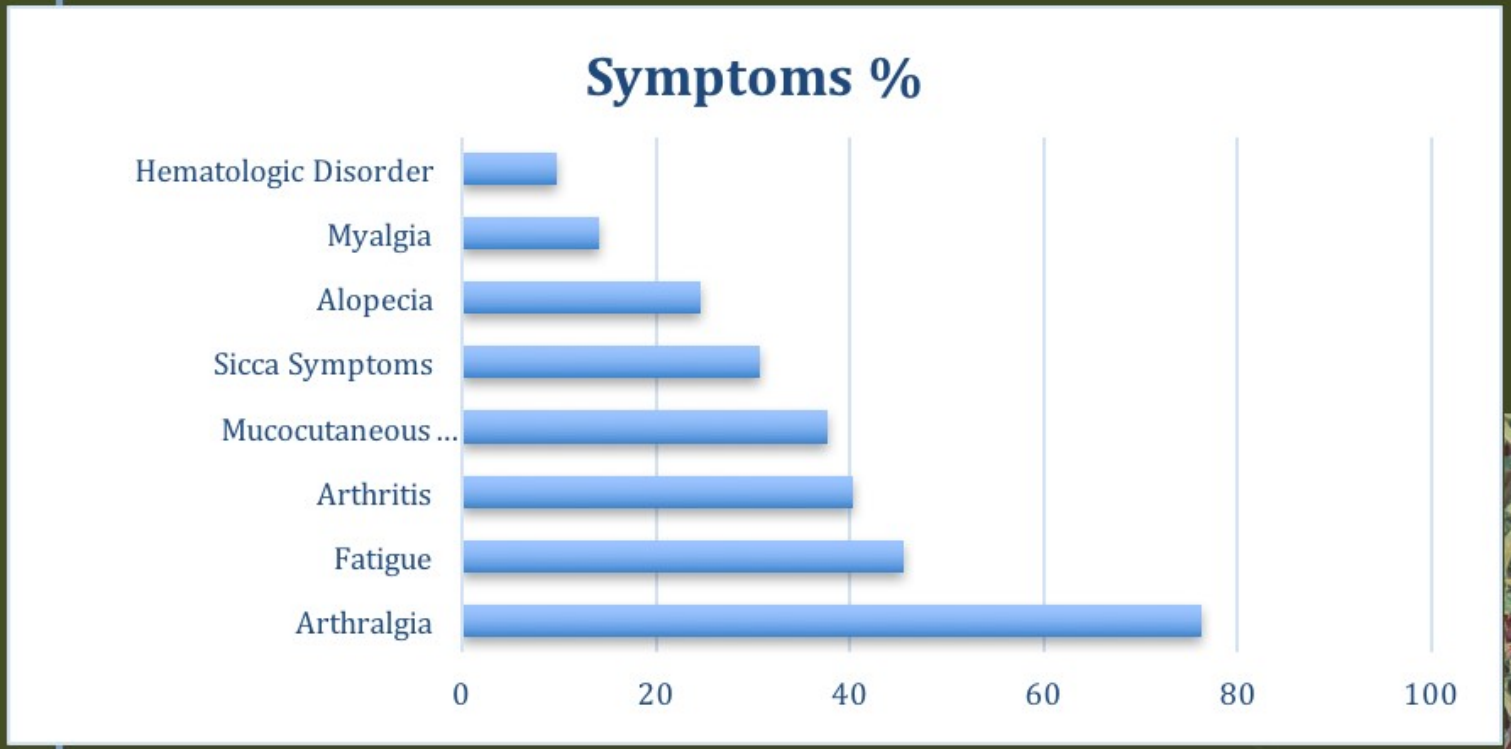
Meeting: 2017 ACR/ARHP Annual Meeting

- Data from this single-center cohort of patients with UCTD show that patients treated with HCQ have multiple clinical criteria and low complement, suggesting that rheumatologists treat pre-clinical autoimmunity in the setting of clinical symptoms.
- Follow-up ANA/dsDNA testing suggests that HCQ may prevent increase in ANA titers or dsDNA autoantibodies and disease progression in UCTD.

Any treatment necessary?

- Symptomatic treatment for presenting symptoms like aches and pain, fatigue, anxiety, some lotion for skin rash may be helpful.
- Some patients may need strong DMARD like Mtx or Lef if symptoms are severe like serositis, persistent arthritis or rash
- Regular check up for organ involvement especially in first 2 years is required to detect development of well-defined CTD and early intervention

Symptoms to care



Regular follow up and tests to catch evolution or need of symptomatic treatment

- Every 6 months for first 2 years
- Every year for next 3 years

Any special care need for pregnancy?

Pregnancy Risk

- More recent studies have provided additional insight into potential risk factors for disease flare and complications of pregnancy in patients with UCTD.
- Having double-stranded-DNA antibodies (based on blood tests done at the beginning of pregnancy) may be associated with an increased risk of disease flare during, and
- having antiphospholipid antibodies may be associated with an increased risk of spontaneous pregnancy loss (miscarriage or stillbirth) in patients with UCTD

Food and Life style
TCL (Therapeutic Lifestyle Chang)

- EIM to regulate and boost immune system
- Avoiding colored food, preserved and ready mades (Chemical)

Summary

- UCTD is much common than CTD, may be all CTD started in stage of UCTD un-diagnosed
- But not all UCTD patients end up with CTD, 1/3 go to CTD, 1/3 had remission and about 1/3 remain in stage of UCTD after 5 years
- Usually not have life threatening organ damage in UCTD stage
- Living healthy life style regular exercise, avoiding triggers like chemicals in environment and food may prevent the progression of autoimmune process
- Symptomatic management and regular check up for timely intervention are essential


THANKS FOR UR
KIND ATTENTION