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@SwastiThinks

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Hello #Nephtwitter #Medtwitter, @ASPNePh Pathology webinar topic for Jan 2022 is Tubulointerstitial Nephritis with Uveitis or #TINU

#ASPNeFOAM #pedneph #Renalpath #Nephpath

But first let's have a poll. Which of the following is true about #TINU?

All the above.

#TINU is a multisystem autoimmune disorder initially described in 2 adolescent girls in 1975 by Dobrin et al. Since then ~600 cases reported.

<https://pubmed.ncbi.nlm.nih.gov/1163543/>

What are some of the risk factors for #TINU?

1. Age: most common in adolescent ♀ but affects all ages
2. Triggers: Infection & drugs
3. Genetic: HLA risk alleles identified: esp HLA-DRB1*01
4. No geographic or racial predilection

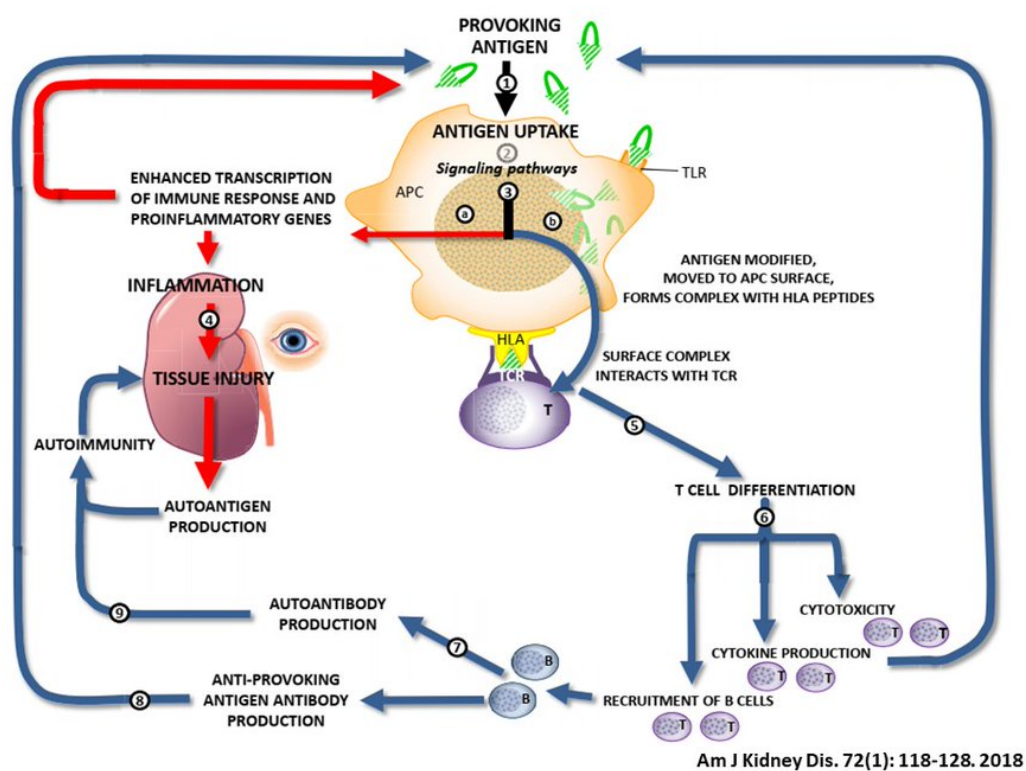
<https://ojrd.biomedcentral.com/articles/10.1186/s13023-017-0677-2>

What is the pathogenesis of #TINU?

#TINU is thought to be an auto-immune inflammatory response to an inciting trigger

Both cellular & humoral immunity pathways activated
Lead to cascade of inflammation in kidney & uvea in genetically susceptible patient

<https://pubmed.ncbi.nlm.nih.gov/29429748/>



Modified CRP (mCRP) may be a target autoantigen in TINU and anti-mCRP antibodies high in # TINU.

<https://pubmed.ncbi.nlm.nih.gov/20813859/>

Kidney involvement can be:

- 🔴🔍 Asymptomatic
- 🔴🔍 Interstitial Nephritis (IN)
- 🔴🔍 Fanconi syndrome
- 🔴🔍 Nephrogenic diabetes insipidus
- 🔴🔍 AKI & CKD
- 🔴🔍 Abnormal urine analysis: ↑ β_2 M, tubular proteinuria/pyuria/haematuria/glycosuria/white cell casts

<https://pubmed.ncbi.nlm.nih.gov/29429748/>

Uveitis is

- ◆ B/L in 80%
- ◆ 2 mo prior to 12 mo post kidney involvement
- ◆ In 52% pts, uveitis after nephritis with an av. delay of 3 mo
- ◆ 80% non-granulomatous anterior uveitis
- ◆ Presents with redness, pain & photophobia
- ◆ 20% posterior or pan uveitis

<https://pubmed.ncbi.nlm.nih.gov/31719109/>



What other systems may be also involved? #TINU can lead to:

- Thyroiditis
- Hearing loss & vestibular failure
- Lymphocytic pulmonary alveolitis
- Other: rash, flu like symptoms, arthritis

<https://pubmed.ncbi.nlm.nih.gov/29429748/>

#TINU is a diagnosis of exclusion

Mandeville et al proposed the diagnostic criteria

<https://pubmed.ncbi.nlm.nih.gov/11738428/>

Box 1 Clinical criteria of acute tubulointerstitial nephritis³

1. Abnormal serum renal function
Increased serum creatinine or decreased creatinine clearance.
2. Abnormal urinalysis
Increased urinary β 2-microglobulin, low-grade proteinuria, presence of urinary eosinophils, pyuria or haematuria without infection, urinary white cell casts or normoglycaemic glycosuria.
3. Systemic illness lasting ≥ 2 weeks
 - i. *Signs and symptoms*: Fever, weight loss, anorexia, malaise, fatigue, rash, abdominal or flank pain, arthralgia or myalgia.
 - ii. *Laboratory findings*: Anaemia, eosinophilia, abnormal liver function or erythrocyte sedimentation rate >40 mm/hour.

<https://pubmed.ncbi.nlm.nih.gov/31719109/>

Table 1 Diagnostic criteria of tubulointerstitial nephritis and uveitis syndrome³

Definite diagnostic	Typical (bilateral anterior) uveitis <i>and</i> interstitial nephritis (renal biopsy <i>or</i> TIN clinical criteria)
Probable diagnostic	Atypical uveitis <i>and</i> positive renal biopsy <i>or</i> typical uveitis <i>and</i> incomplete TIN criteria
Possible diagnostic	Atypical uveitis <i>and</i> incomplete TIN clinical criteria

TIN, tubulointerstitial nephritis.

<https://pubmed.ncbi.nlm.nih.gov/31719109/>

#TINU may be under-recognised due to:

- ✚ Absence/asynchrony of eye and kidney symptoms
- ✚ Kidney symptoms commonly come 1st & may resolve before uveitis
- ✚ Uveitis may be asymptomatic
- ✚ Steroids used to treat kidney disease may mask uveitis

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5873972/>

Recent standardization of nomenclature (SUN): using 1083 cases of anterior uveitis, including 94 cases of TINU, evaluated by machine learning may be helpful.

<https://pubmed.ncbi.nlm.nih.gov/33845023/>

TABLE 3. Classification Criteria for Tubulointerstitial Nephritis With Uveitis Syndrome	
Criteria	
1. Evidence of anterior uveitis	
a. Anterior chamber cells	
b. If vitritis or choroiditis or retinal vascular changes are present, anterior chamber inflammation also should be present	
AND	
2. Evidence of tubulointerstitial nephritis, either	
a. Positive renal biopsy OR	
b. Elevated urine β -microglobulin and either abnormal urine analysis or elevated serum creatinine	
Exclusions	
1. Positive serology for syphilis using a treponemal test	
2. Evidence of sarcoidosis (either bilateral hilar adenopathy on chest imaging or tissue biopsy demonstrating noncaseating granulomata)	

<https://pubmed.ncbi.nlm.nih.gov/33845023/>

Some other differential diagnosis to consider for multisystem kidney & eye disease

1. Autoimmune: Sjogren, JIA, Behcet's
2. Vasculitis: SLE, granulomatous polyangiitis
3. Infection: TB, Syphilis
4. Other: Sarcoidosis

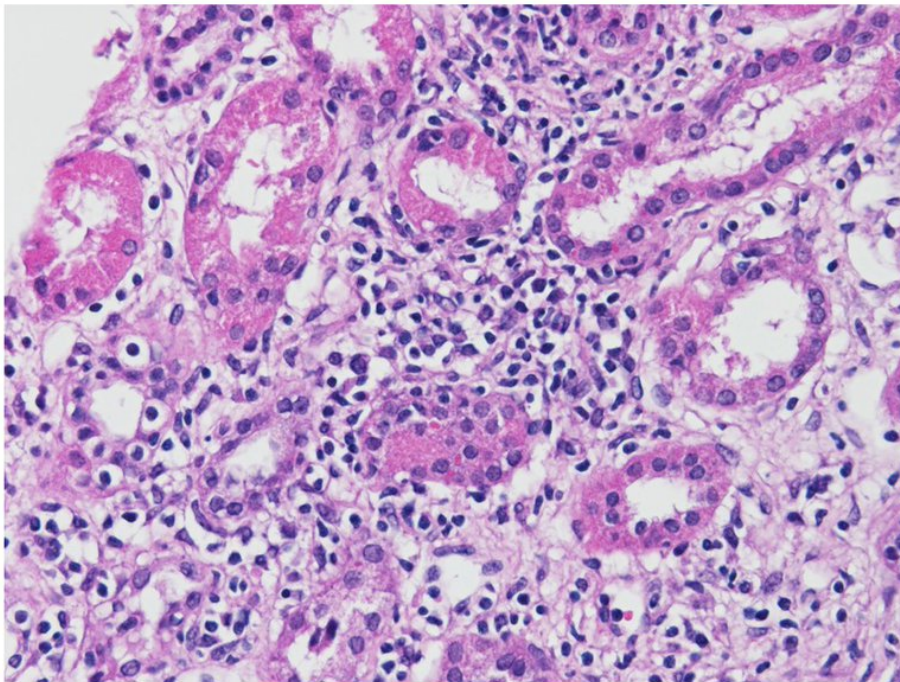
<https://pubmed.ncbi.nlm.nih.gov/29429748/>

Kidney Biopsy in #TINU shows

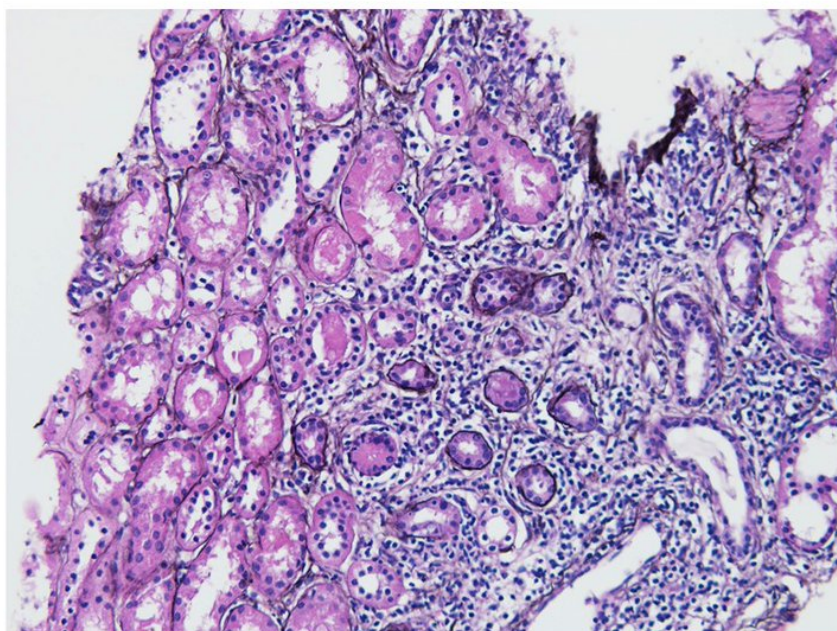
- Interstitial oedema
- Inflammatory infiltrate composed mostly of lymphocytes
- Tubular injury

<https://pubmed.ncbi.nlm.nih.gov/28532639/>

TINU with interstitial lymphocytes, occasional plasma cells, and tubulitis with associated interstitial edema (hematoxylin and eosin stain). <https://pubmed.ncbi.nlm.nih.gov/28532639/>



TINU with interstitial inflammation out of proportion to tubular atrophy, with early interstitial fibrosis and interstitial edema (Jones silver stain). <https://pubmed.ncbi.nlm.nih.gov/28532639/>



Treatment of #TINU?

- ✂️ Topical steroids & cycloplegic agents in eye
- ✂️ Systemic steroids: 1mg/kg/day for 3-6 mo in most studies
- ✂️ Evidence for IMT (immunomodulatory Rx) in TIN is limited: may include AZA, MMF, CNI, Biologics

<https://iovs.arvojournals.org/article.aspx?articleid=2270915>

Prognosis of TIN

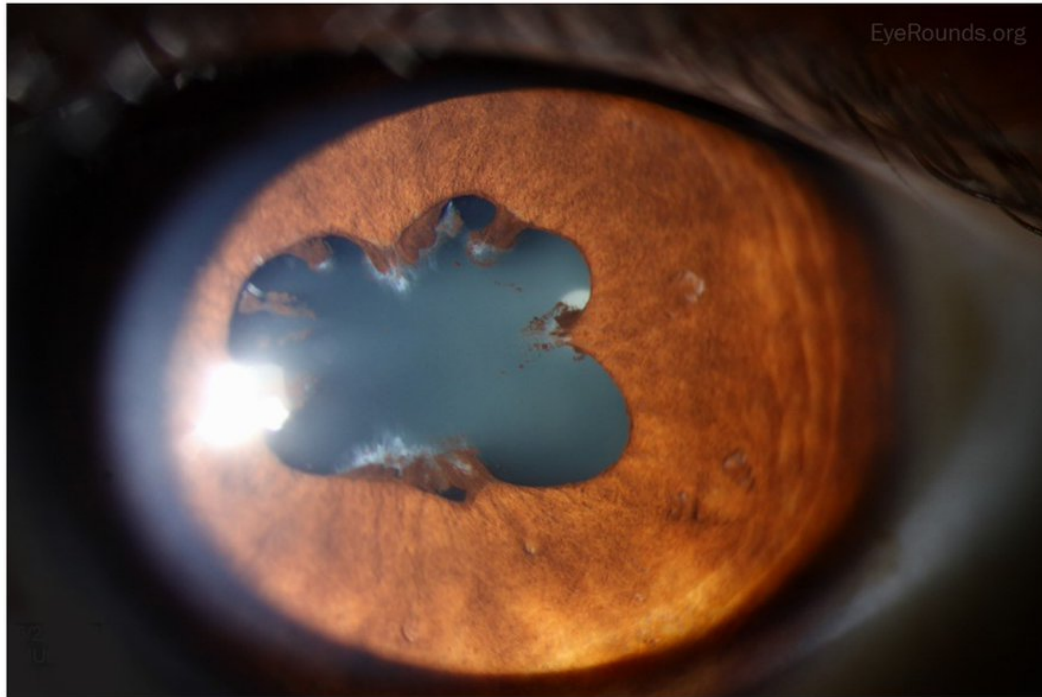
- AKI & CKD more common in adults
 - ~10% children and ~40% adults develop CKD
 - Can recur post-transplant
 - Urine β_2 M levels may help in therapeutic decisions

<https://pubmed.ncbi.nlm.nih.gov/33561271/>

Prognosis of uveitis

- Relapses and chronicity in 50%
- Children have more severe eye disease and relapses
- Can lead to reduced visual acuity
- Complications in ~ 20%: post synechiae, macular & disc oedema, chorioretinal scarring

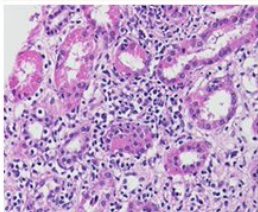
<http://EyeRounds.org/cases/226-TINU.htm>



Here is the summary of our discussion so far..

TUBULOINTERSTITIAL NEPHRITIS WITH UVEITIS #TINU

A multisystem autoimmune inflammatory disorder of unknown etiology



Risk Factors

- More common in adolescent females but can occur at any age
- No geographic or racial predilection
- Genetic: HLA risk alleles identified: particularly HLA-DRB1*01
- Triggers: Infection & drugs (NSAID's, antibiotics, Chinese herbal medicines)

Clinical Features

- Uveitis: Painful red eyes, often bilateral, 2 mo prior to 12 mo post kidney involvement
- Kidneys: TIN, AKI, CKD
- Other: anorexia, weight loss, rash, arthralgia, thyroiditis, SN hearing loss, alveolitis

Diagnosis

- Blood tests: elevated creatinine, anaemia, raised ESR
- Urine: sterile pyuria, increased β_2 microglobulin. Kidney Biopsy: definitive: lymphocytic TIN
- Rule out other causes of kidney & eye disease: Sjogren, SLE, Sarcoidosis

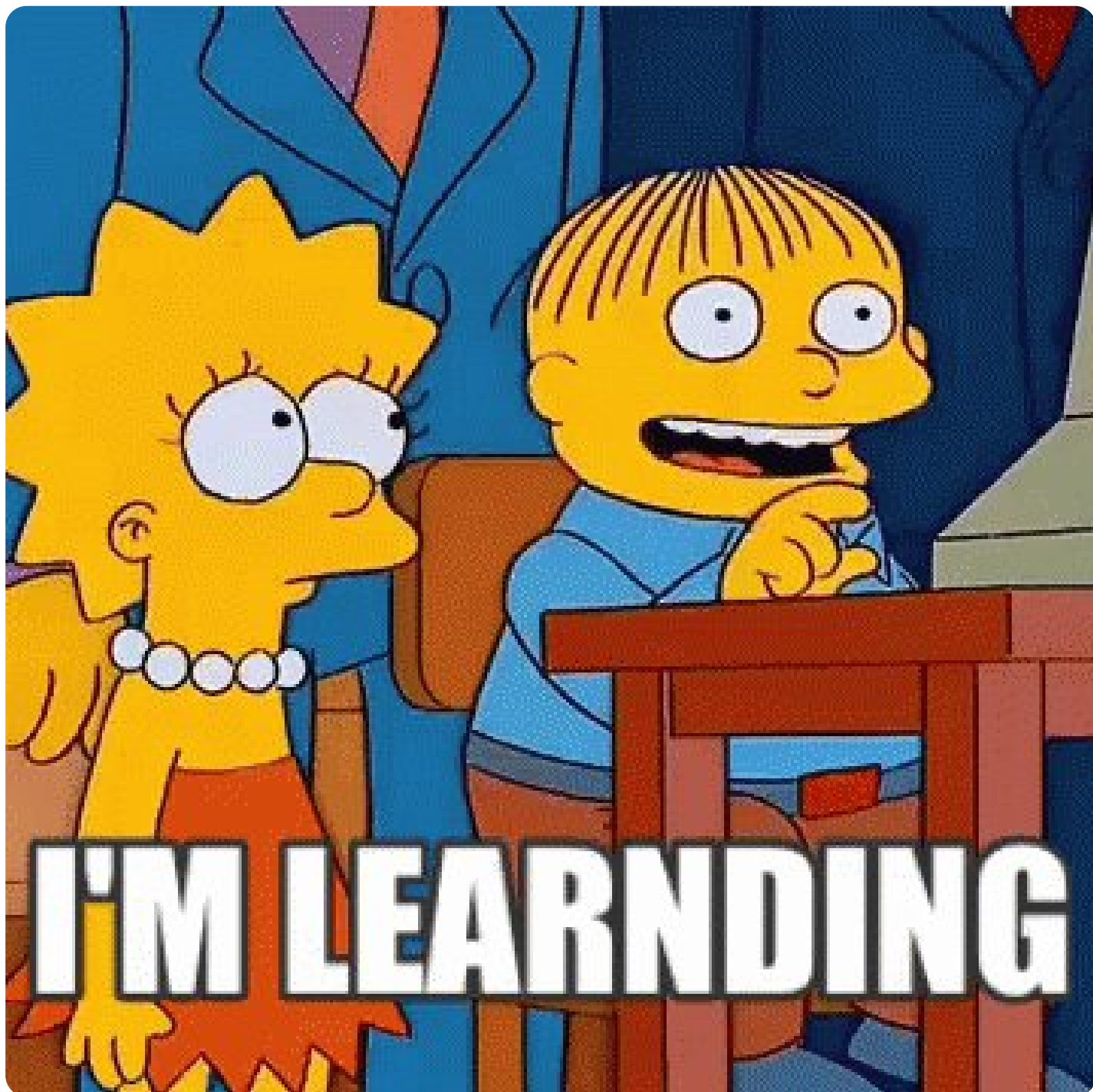
Treatment & Prognosis

- Corticosteroids. Second line: Methotrexate, azathioprine, MMF, biologics
- ~10% children and ~40% adults develop CKD
- Relapses of uveitis more common in children and can lead to permanent damage

Infographic by Swasti Chaturvedi [@SwastiThinks](#)

For a case-based clinical discussion with a pathology expert
login to @ASPNePh website, Jan webinar #Membereducation

Special thanks to #ASPNePh @drM_sudha @nefron1310



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