

Disease Morbidities 2; IgM related disorders, renal, hyperviscosity & Cryos

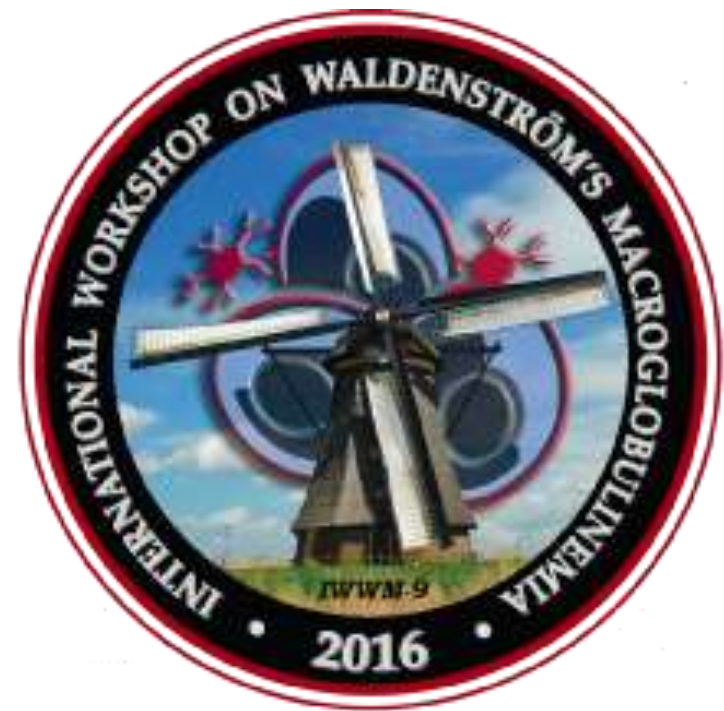
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St Antonius Ziekenhuis Utrecht/Nieuwegein

Patientendag Waldenstrom workshop 2016

**9th International Workshop on Waldenström's
Macroglobulinemia and Symposium on Advances in Multiple
Myeloma
Amsterdam, The Netherlands, October 5-8, 2016**

**We had an amazing conference:
Thank you everyone!**



Rembrandt van Rijn 1606-1669 – Anatomy Lesson



Dokter Tulp

Complications of WM

- **IgM related disorders: even when there are not many tumour cells, the IgM can still be tricky**
- **Hyperviscosity – when the blood is too sticky**
- **Cryo's: when the blood clots in cold**
- **Renal disease related to WM: can the kidneys suffer from WM?**

IgM related Disease

- **Waldenstrom's disease: high tumor load in the bonemarrow, high IgM; symptoms arise because of the tumour (i.e. anemia, hyperviscosity)**
- **IgM related disease: low/no tumor load in the bonemarrow, low IgM but this little bit of disease leads to (sometimes severe) symptomes**
“dangerous small clone” .

Types IgM related disease (typically IgM MGUS)

- **Deposition diseases:**

- amyloidosis, light chain deposition, IgM depositon

Neuropathy

Nephropathy- kidney disease

Cryo's

Cold agglutinins

Schnitzler syndrome (skin)

How to treat

- Depends on the type of IgM related disorder
- Most will be discussed today

Hyperviscosity

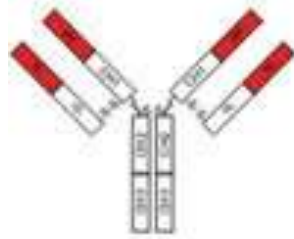
Probably the most dangerous complication of WM

What is viscosity



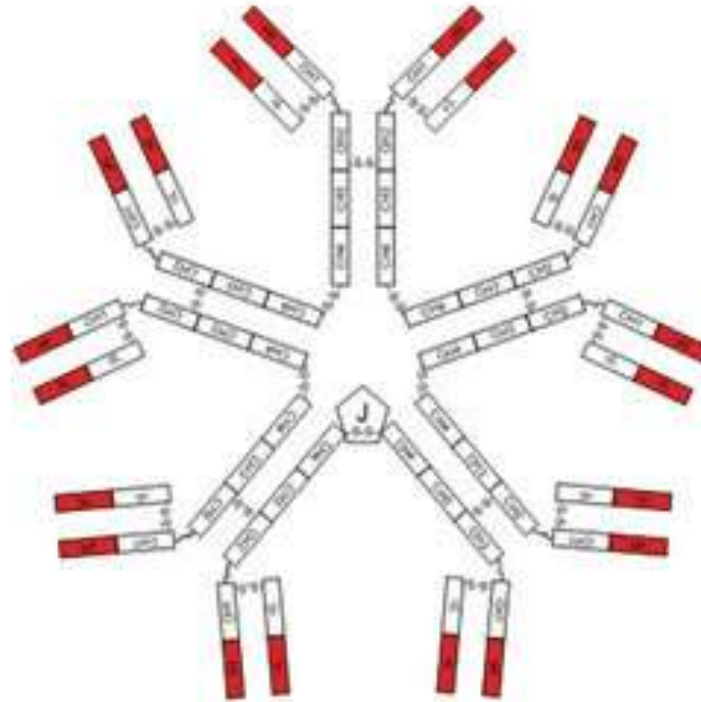
Let's remember: why is it called macroglobulinaemia? Because it's so big!

(A) IgG



~150 kDa

(B) IgM (pentamer)



~950 kDa

Hyperviscosity syndrome

- Described in 1944 in the initial 2 patients identified by J.G. Waldenstrom
- High IgM makes the blood too thick
- mostly at IgM > 6 g/dL- 60 g/L but possible from 3 g/dL – 30 g/L)
- This can lead to
 - Bleeding (nose, other mucous membranes, skin)
 - Retinopathy – damage to the retina in the eye
 - Neurological problems

Symptoms and signs: sausaging of the retinal vessels – hotdogs on a string



How to diagnose

- IgM paraproteine
- Viscosity testing of the blood (although....)
- Clinical awareness of symptoms
- Funduscopy (“ eye exam”)

How to treat?

- Plasmaferesis!
- “ Wash” the blood to filter out the IgM
- Via central line



For how long

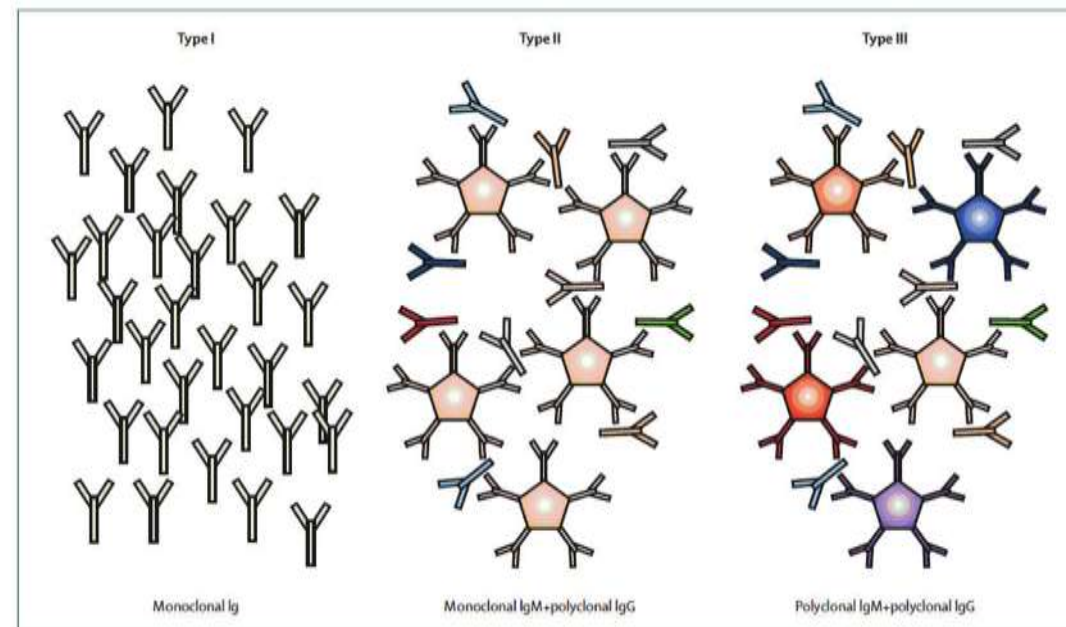
- Sessions every day-couple of days-weekly
- Untill the IgM is brought down by rapid acting treatment

New during IWMM9

- No new insights, but more and more rapidly effective agents available!

What are cryoglobulines?

- Proteins that precipitate in cold circumstances
- Typically, 3 types are distinguished:
 - Type 1: monoclonal IgM or IgG -> WM/IgM MGUS, other lymphoma's
 - Type 2: monoclonal IgM with polyclonal IgG -> hep C
 - Type 3: polyclonal IgM/IgG -> auto-immune diseases (lupus, RA)
- **Type 1: WM/MGUS, lymphoma**
- **Type 2/3: Hepatitis C, autoimmune diseases (lupus, RA), But sometimes also lymphoma**



WARM



COLD



Anecdote courtesy
of dr Marvin Stone

Symptoms of cryo's



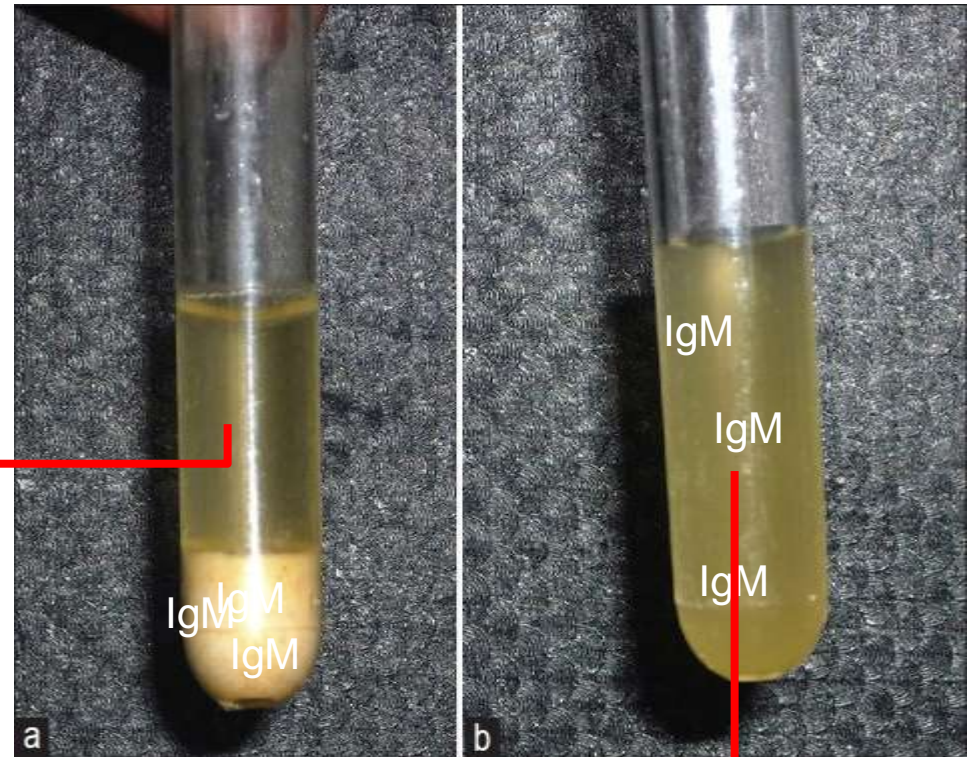
- Purpura
- Acrocyanosis
- Ulcera-poor wound healing
- Mostly on extremities- where the vessels are small and the blood cools (shins, ears, nose, fingertips)



Cryoglobulines

Can falsely lower the IgM when not testing in warm bath!!

(or in warm room – dr Eva Kimby, Karolinska institute Stockholm, Sweden)



Paraproteine:
negative!

Paraproteine test:
positive!

Complications of cryo's

- Mild symptoms (most frequent)
- purpura (bright red circles, from the size of a pinhead up to half an inch)
- Poor wound healing
- Kidney problems
- Hyperviscosity (because of the immune complexes/precipitation)
- Joint pain/swollen joints
- Neuropathy

What can you do about cryo's?

- **Stay warm**
- **Take care / keep an eye on ulcers or wounds**
- Inform your physician/nurse if you have cryo symptoms
- Sometimes hep C needs to be tested

- Mild -> wait & see, monitoring
- Severe
- -> treatment of underlying disease
- -> sometimes pheresis (in a warm room!)

New during IWWM9

- We now know there's a warm room in Karolinska institute!

WM related nephropathy

- Kidney complications related to WM

Medicine in the Dutch Golden Age

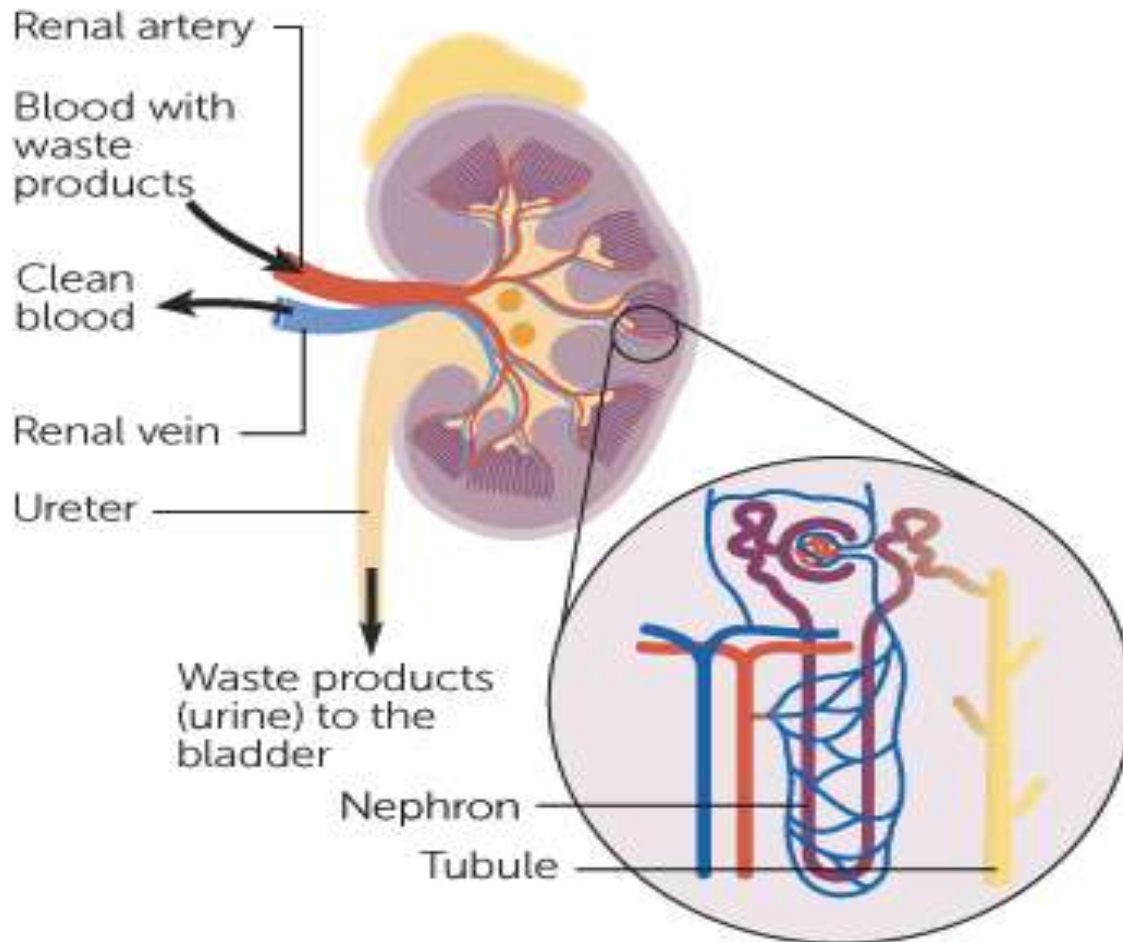
Gerard Dou 1613-1675 :

The Physician



Why check urine in
WM?

The kidney filters the blood: 1 liter/minute!



Cancer Research UK

Renal complications in WM

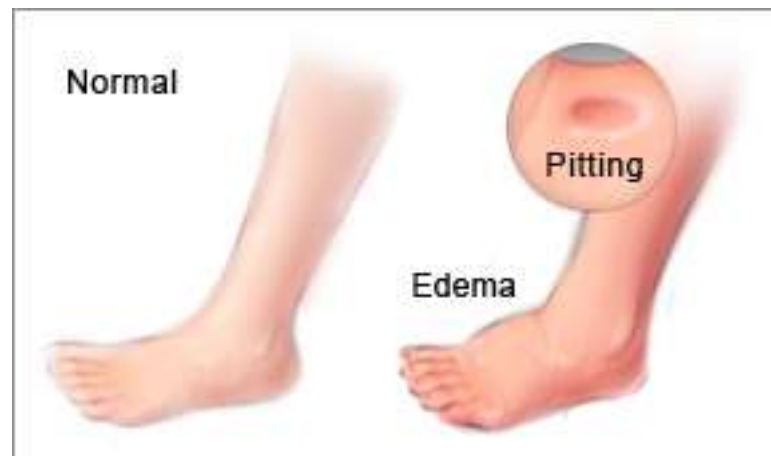
- Up to 5% of patients on 15 years of follow up
- Great variety in WM related renal disease
- Renal disease is not always related to WM! (Diabetes, hypertension)
- Sometimes a biopsy of the kidney will be needed to determine the cause

1) Chauvet et al AJKD 2015, 2) Vos et al, BJH 2016

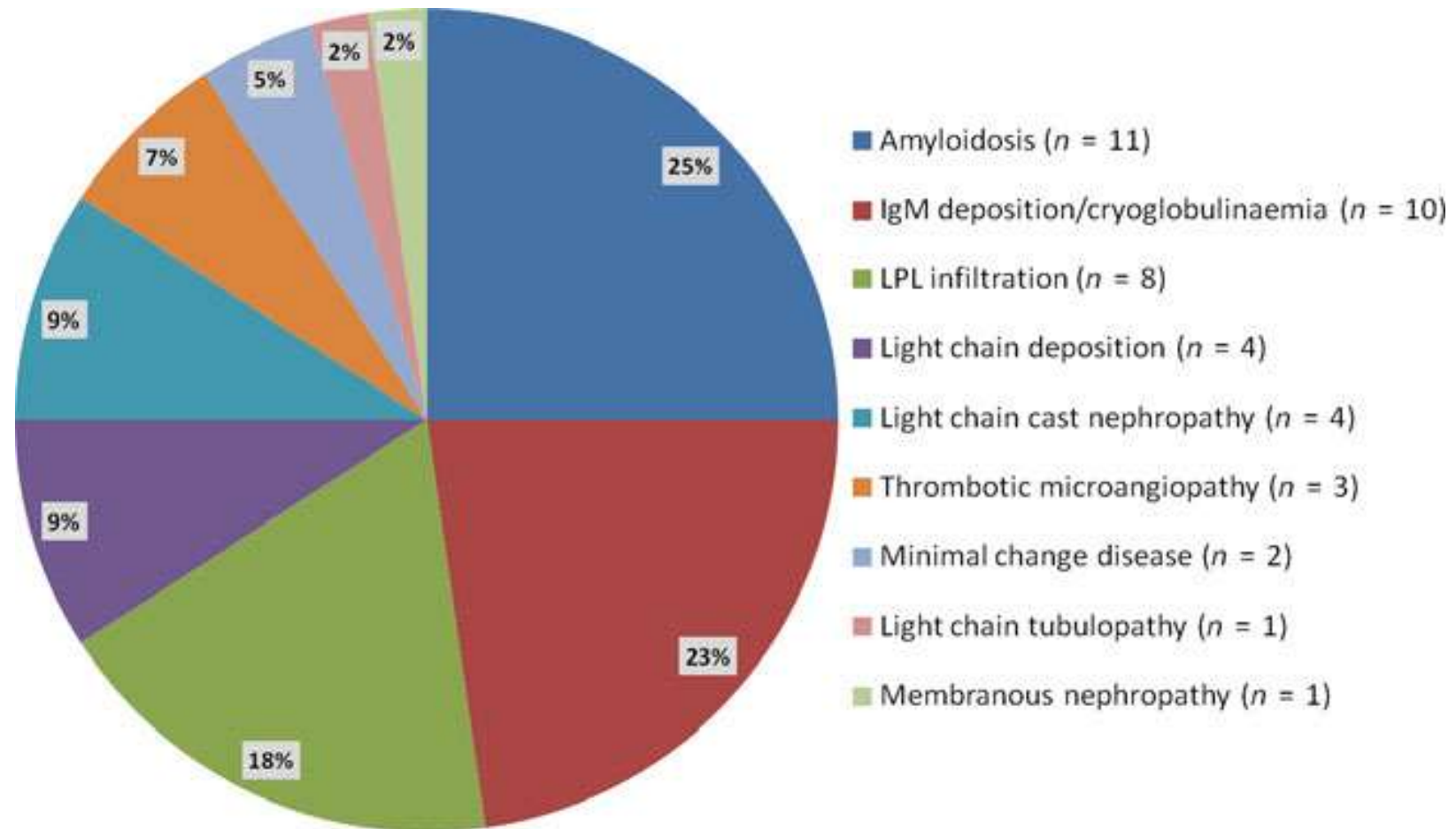


What are the symptoms of renal disease

- Renal failure – no symptoms until it's very advanced (fatigue, not feeling well)
- Nephrotic syndrome (protein leakage) – edema also in the face
- “tubulopathy” – disturbances in the salt in the blood – muscle cramps, typically asymptomatic and picked up by routine lab



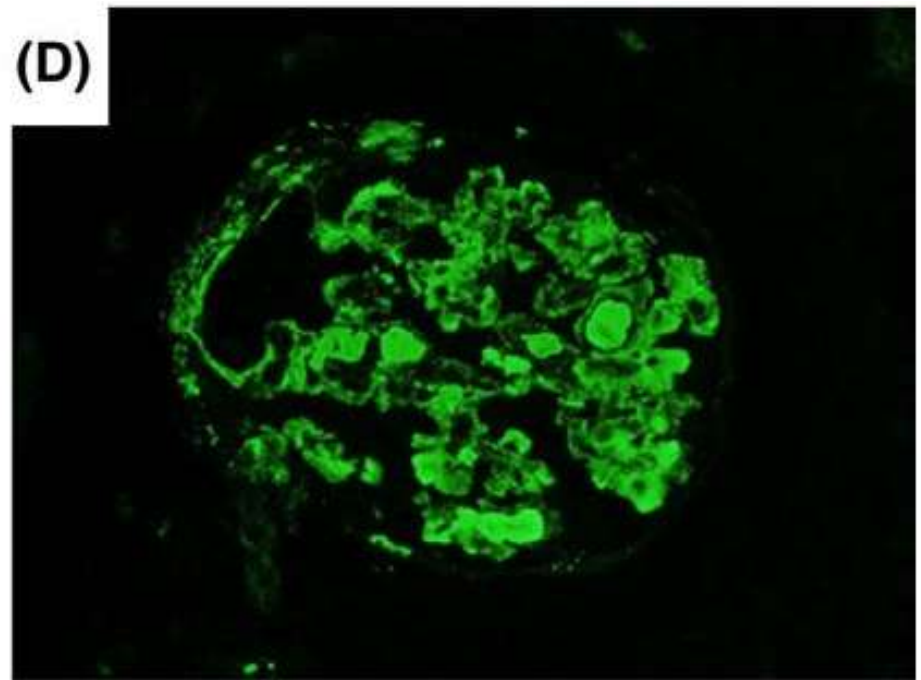
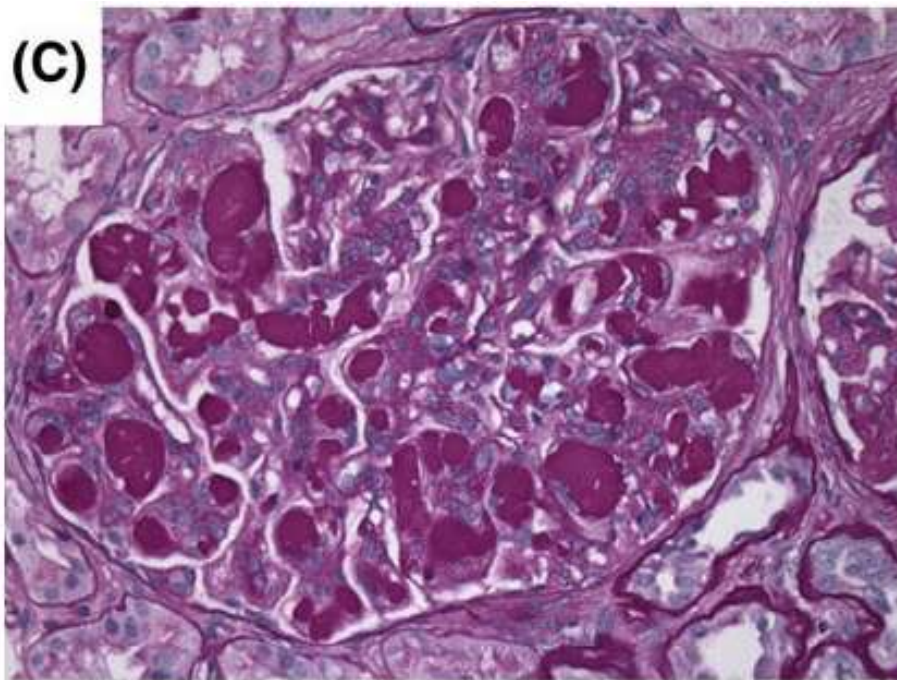
Renal complications in WM: many different types; based on kidney biopsies



What else do we know

- 50% of cases diagnosed together with WM diagnoses, but can occur up till 10 years later
- WM'ers with kidney complications have somewhat poorer outcomes
-
- If renal function is saved then outcomes are better
- Hematologist/oncologist needs to cooperate closely with kidney specialist (nephrologist)
- Optimal treatment unknown and very dependent on exact type of kidney disease

Monoclonal IgM deposition disease (



Often mild clinical course
with relapses over the
years

What can you do about kidney complications

- Monitoring kidney function (typically part of standard blood testing)
- Check the urine for proteins
- Be aware of symptoms (only nephrotic syndrome)
- Doctors should be aware this can be associated with WM/IgM MGUS and make the proper investigations

New on IWWM9

- Recent published analysis of data from the Bing Center cohort was discussed (based on 1391 WM patients)

Thank you & enjoy your time in The Netherlands

Gerard Dou's doctor is @
Rijksmuseum, Amsterdam

Rembrandt's Anatomy lesson is
@ Mauritshuis, The Hague.



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