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

Josephine MI Vos, MD
St Antonius Ziekenhuis Utrecht/Nieuwegein
Patientendag Waldenstrom workshop 2016

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We had an amazing conference:

Thank you everyone!

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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

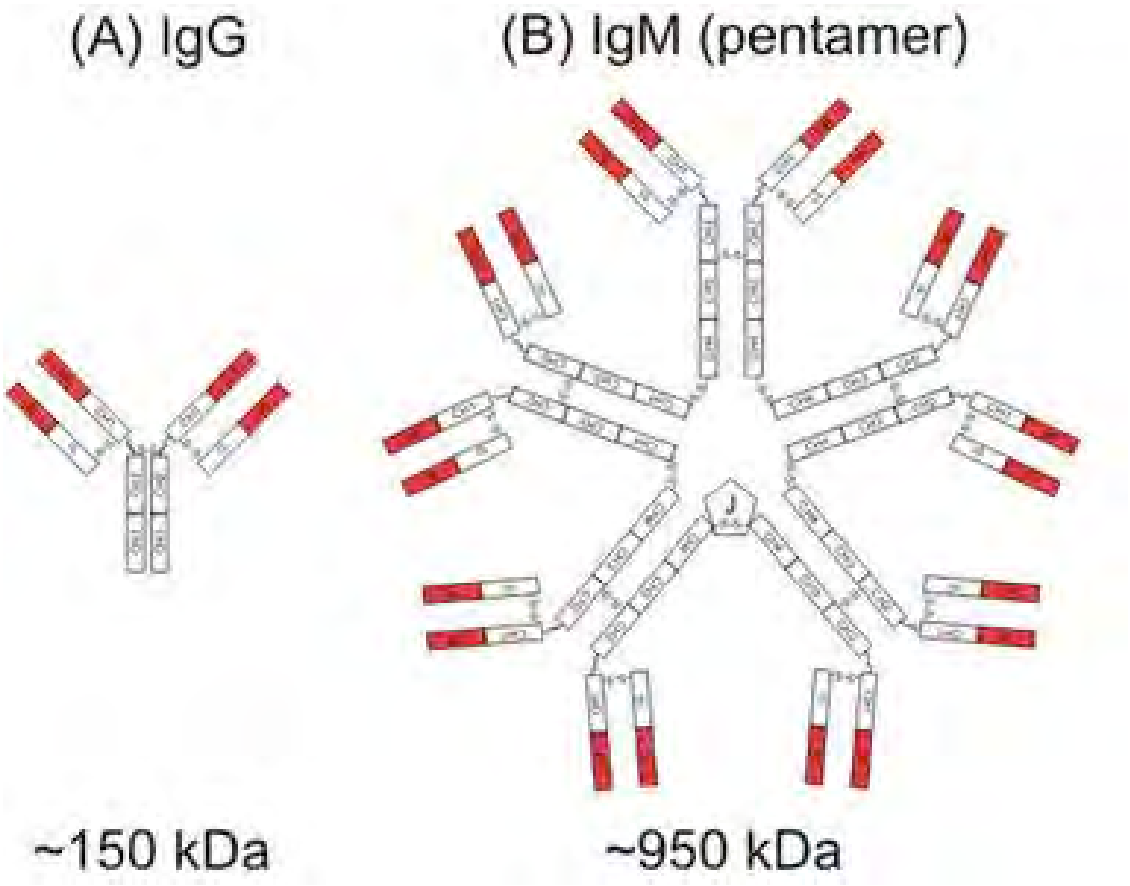
- Depends on the type of IgM related disorder
- Most will be discussed today

Hyperviscosity

Probably the most dangerous complication of WM

What is viscosity

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



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: sausasing 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**

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For how long

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

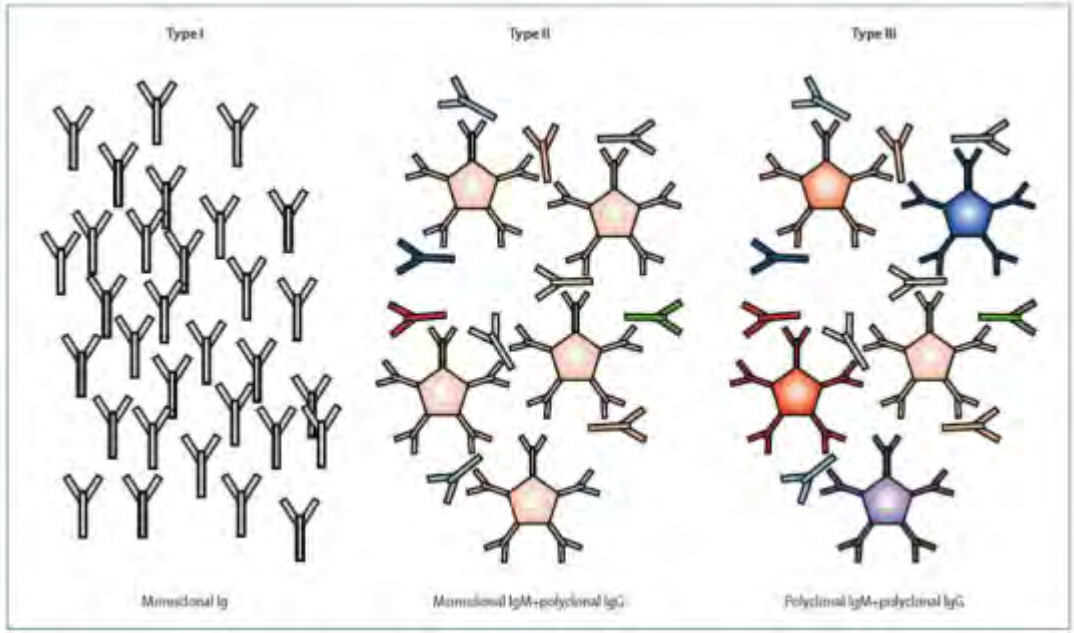
New during IWMM9

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

What are cryoglobulines?

- **Proteins dat 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

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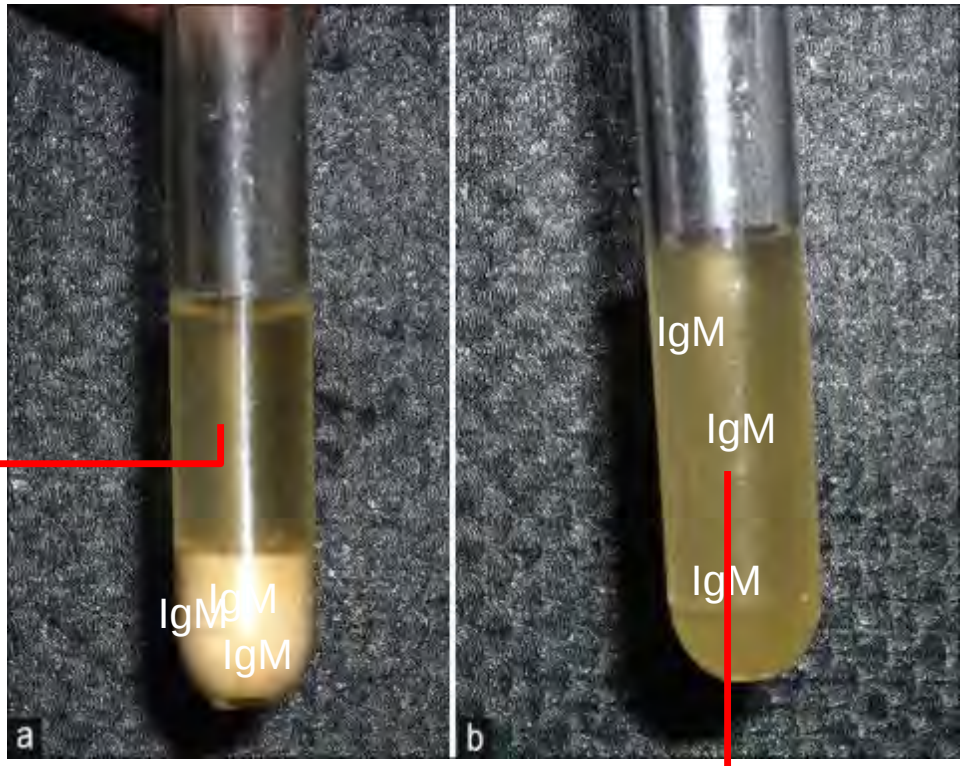
Symptoms of cryo's

- 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!

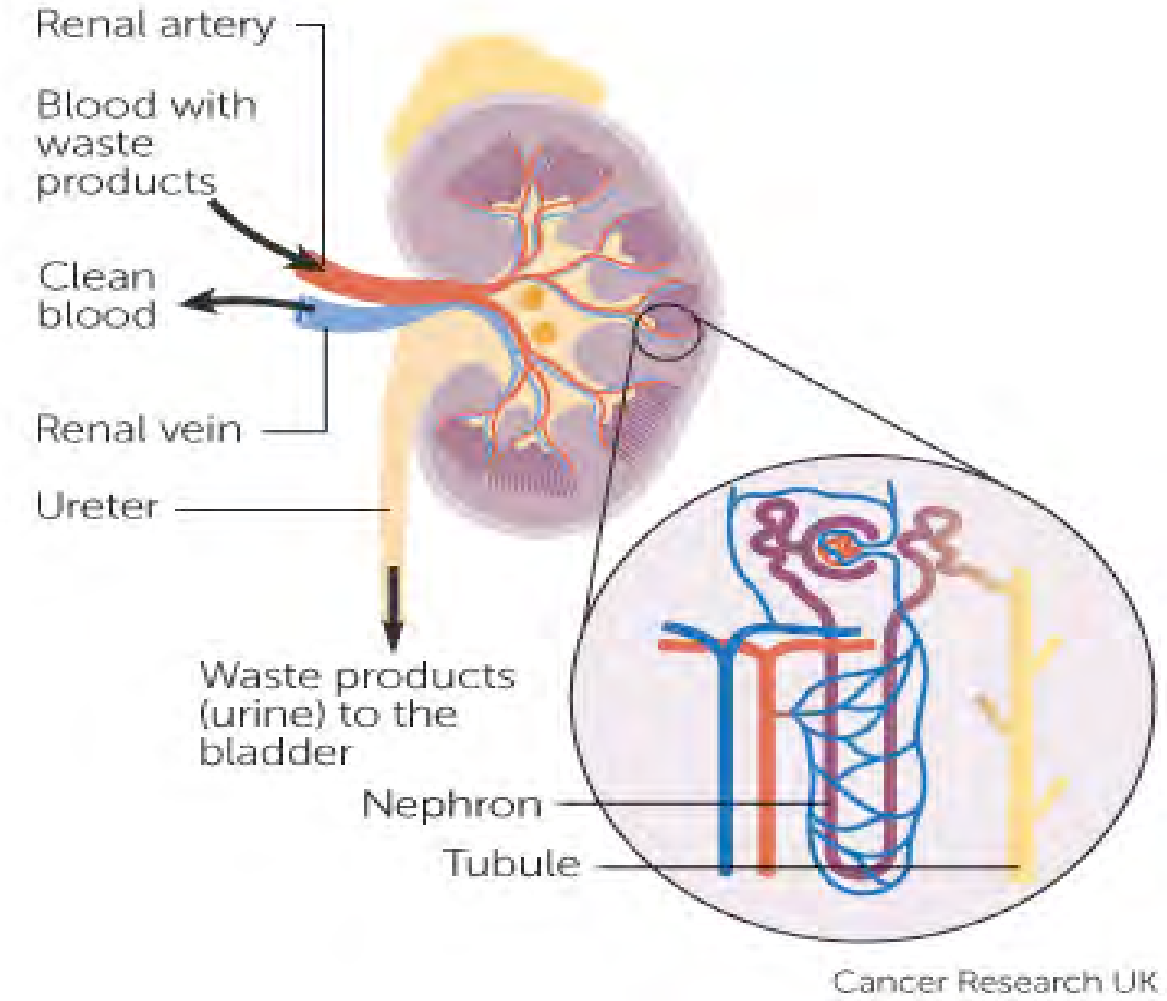
WM related nephropathy

- 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!



Renal complications in WM

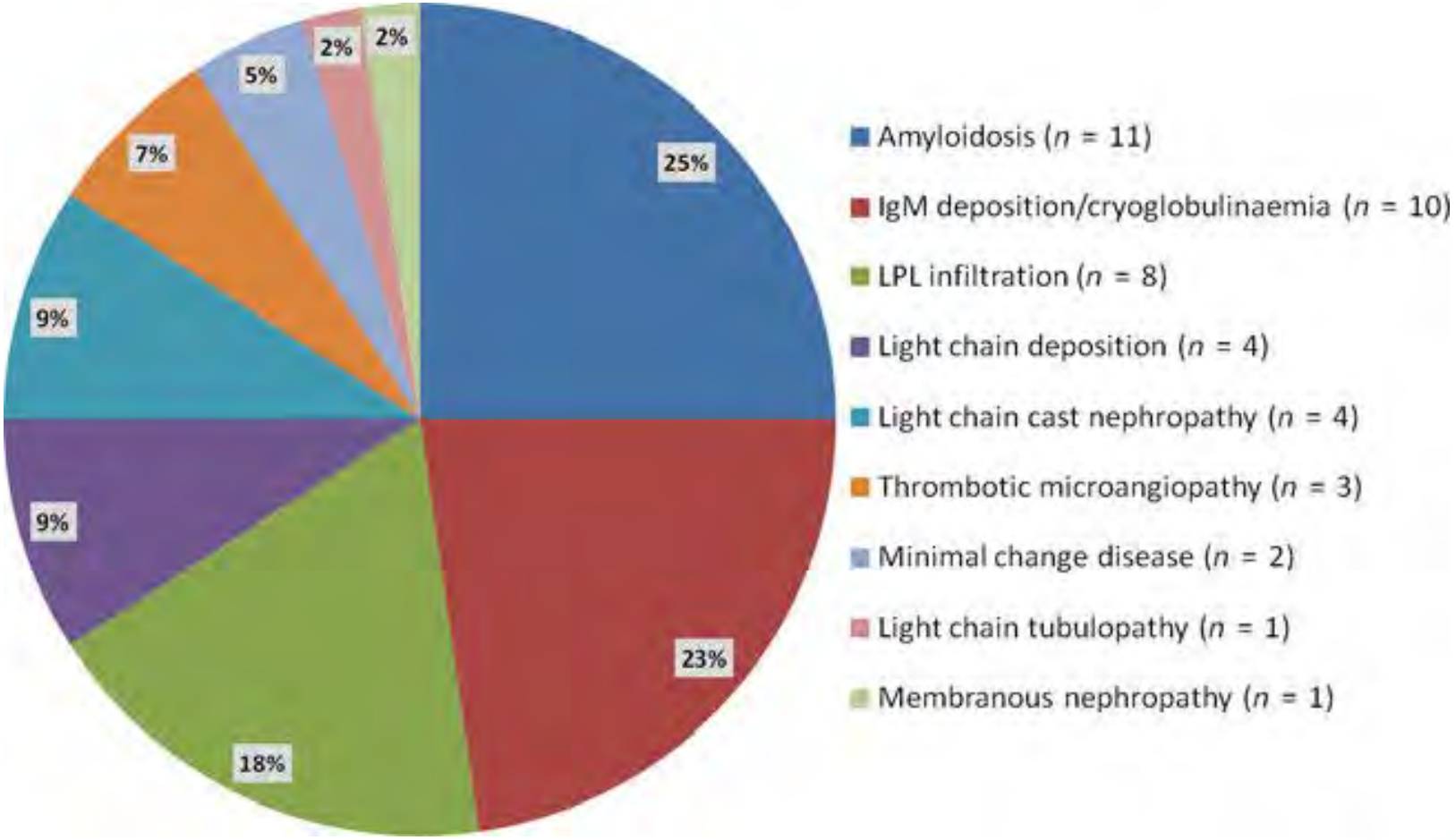
- Up to 5% of patients on 15 years of follow up
- Great variety in WM related renal disease
- Renal disease is not always related to WM! (Diabetes, hypertension)
- Sometimes a biopsy of the kidney will be needed to determine the cause

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

What are the symptoms of renal disease

- Renal failure – no symptoms untill it's very advanced (fatigue, not feeling well)
- Nephrotic syndrome (proteine 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



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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
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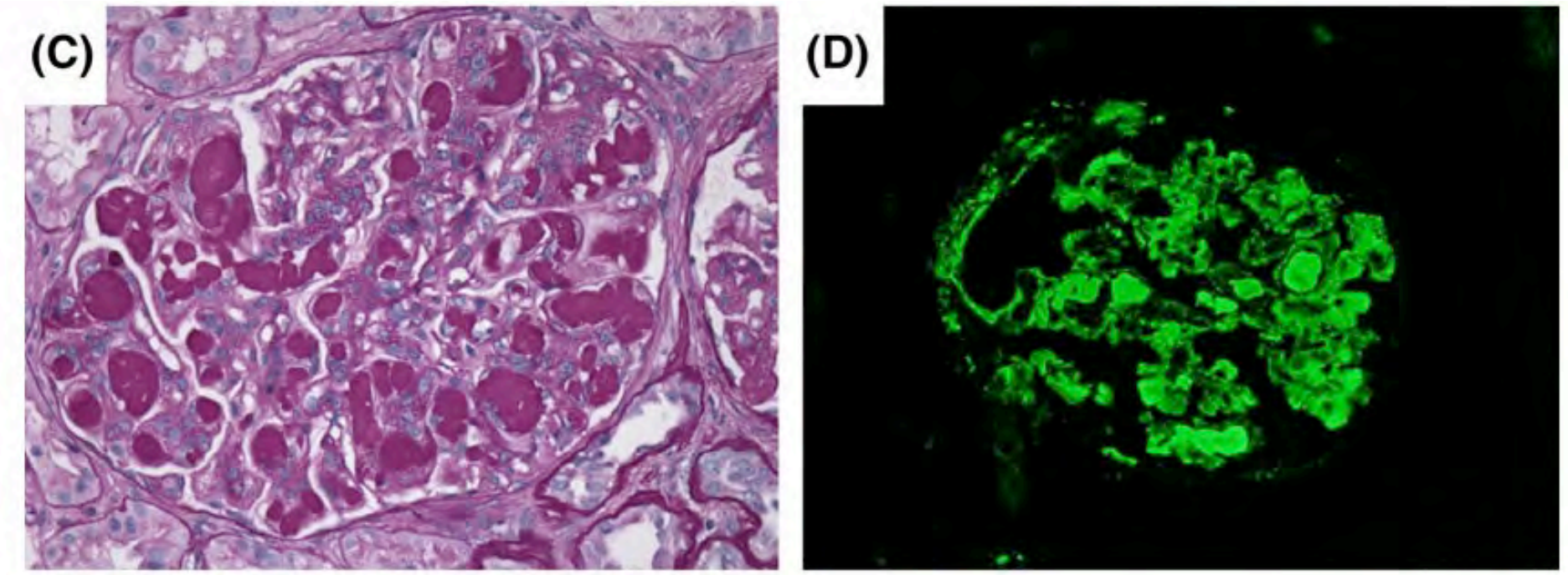
- If renal function is saved then outcomes are better
- Hematologist/oncologist needs to cooperate closely with kidney specialist (nephrologist)
- Optimal treatment unknown and very dependent on exact type of kidney disease

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 proteine
- 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.