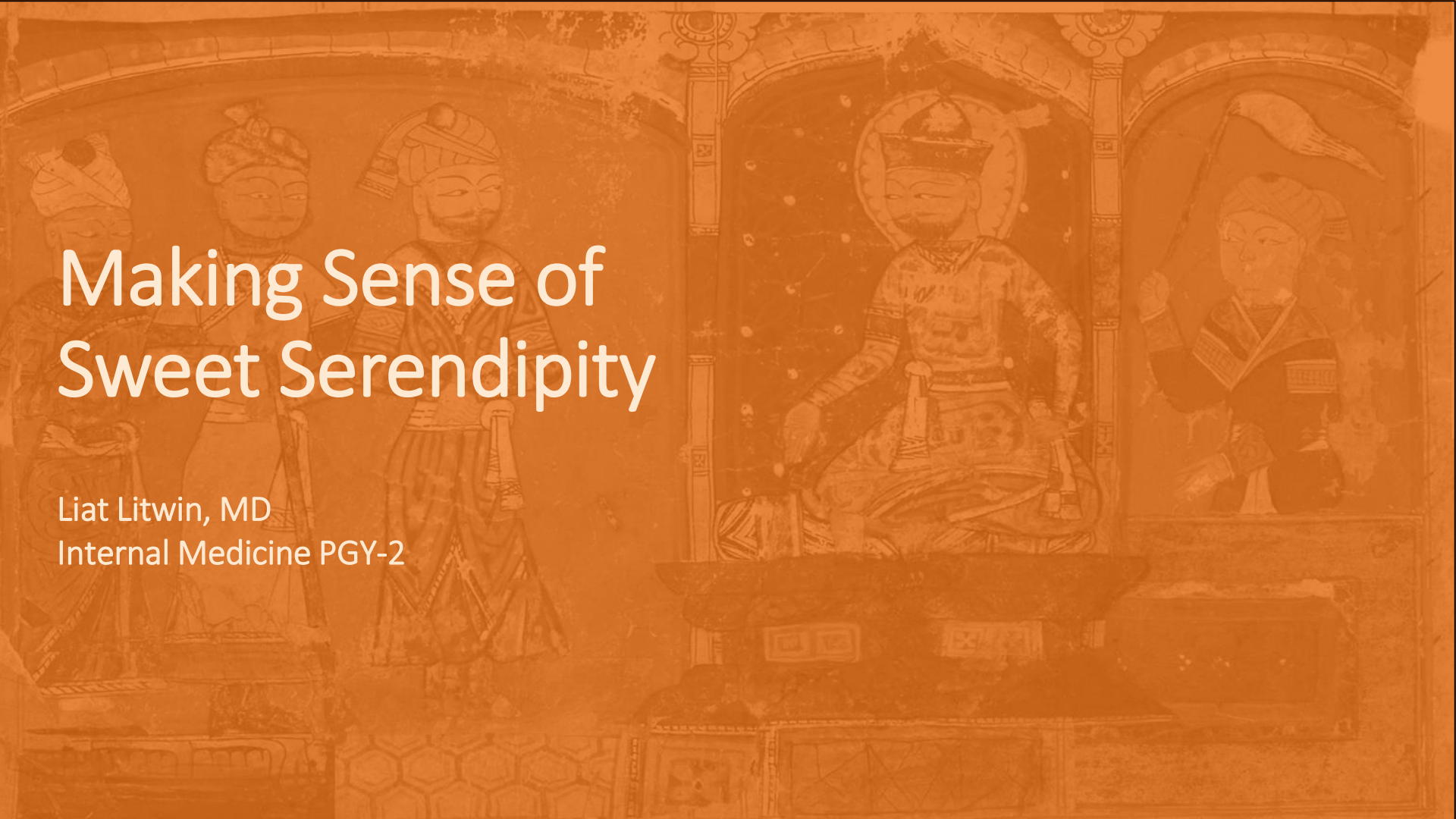


Making Sense of Sweet Serendipity

Liat Litwin, MD
Internal Medicine PGY-2

The Patient

A 67-year-old man was admitted with **acute generalized weakness**. Endorsing one day of myalgias, urinary retention, and dysphagia.

Medical and social history

- Insulin dependent diabetes mellitus (HbA1c 10%)
  - Insulin glargine 70U daily, glipizide, metformin
  - Diagnosed 15 years prior
  - A1C ranging 7-10% over past several years
- CKD type 3
- HIV on HAART
- Recent 7 day admission for cough, nausea, vomiting, diarrhea during which given 7 day course of treatment for CAP and supportive treatment
- Discharged 1 day prior to re-admission

Hospital course

CSF: WBC 12, RBC 1, Protein 25, Glucose 50, negative gram smear, negative culture, negative cryptococcal Ag

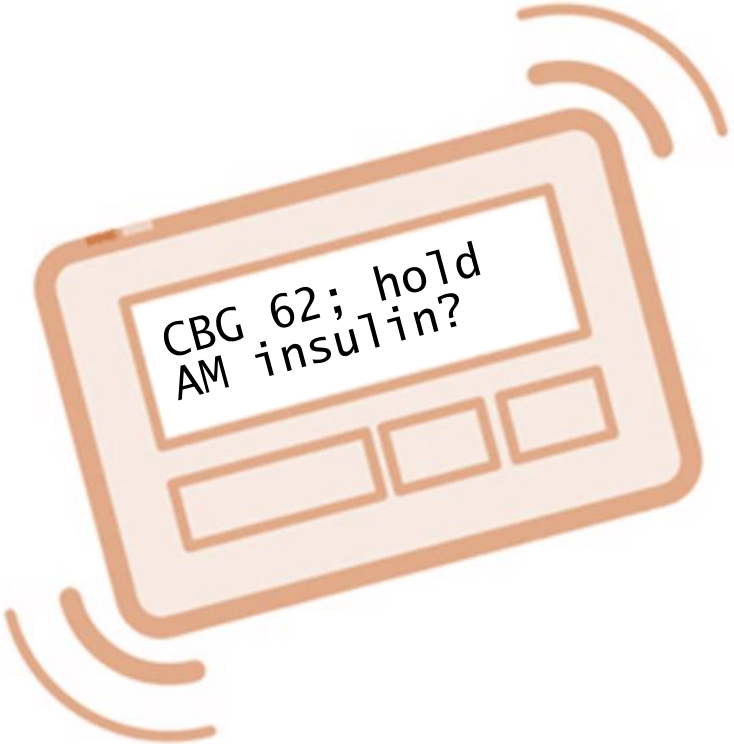
JCV: negative, **CMV:** negative, **Crypto ag:** negative
Homocysteine: 9.5, **MMA:** 117

MRI total spine: no evidence of cord signal changes or enhancement

Worsening weakness, new oxygen requirement

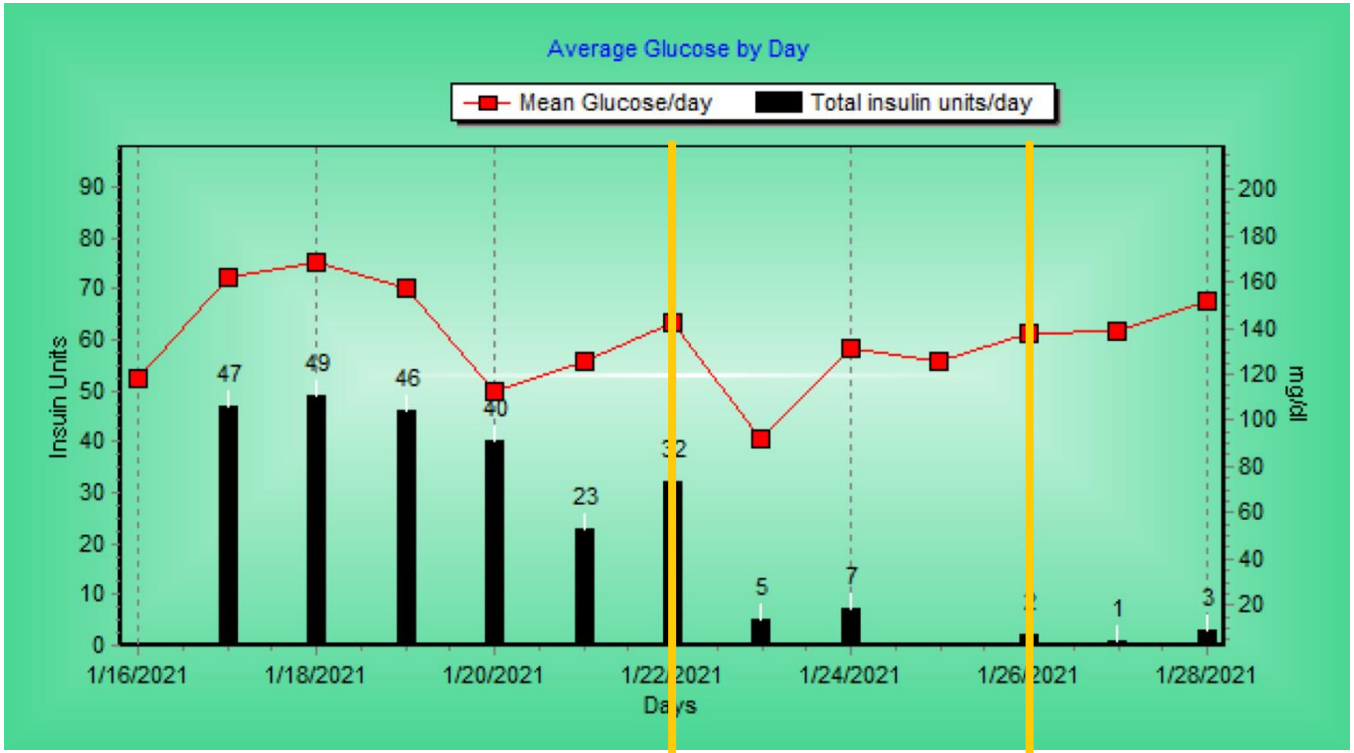
Decision to empirically treat with IVIg 2gm/kg for 5 days

“Atypical Guillain Barré Syndrome”


CBG 62; hold
AM insulin?

The following day, this happened again

And this pattern persisted:



What was going on?

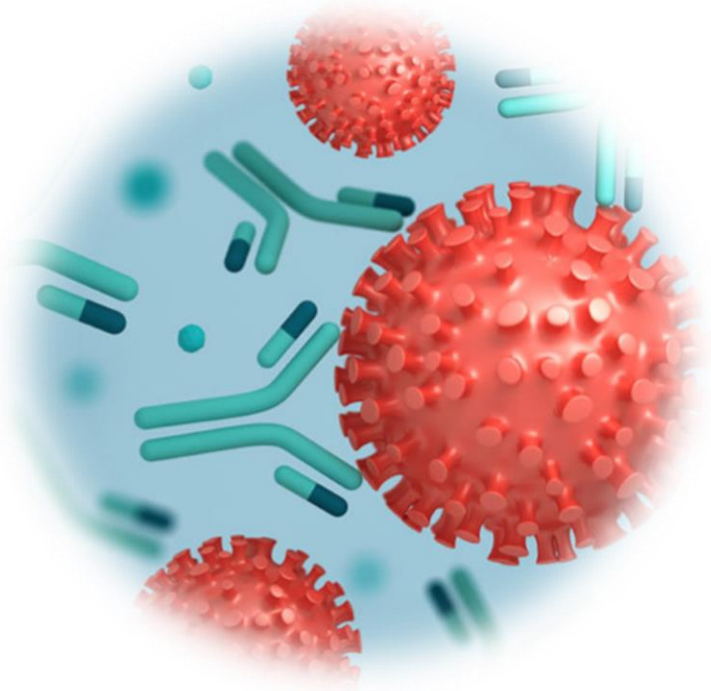
67-year old man with a history of poorly controlled DM2, who was admitted for treatment of an atypical Guillain Barré syndrome, and found to have reduced insulin requirements following treatment with IVIg.

Revisiting the basics

- Type 1 – auto-immune
- Type 2 – “insulin resistance”
- Pancreatogenic
- Maturity onset diabetes of the young (MODY)
- Latent autoimmune diabetes in adults (LADA)

Could he have had an undiagnosed auto-immune diabetes?

- **GAD antibody:** negative
- **Insulin receptor antibody:** negative



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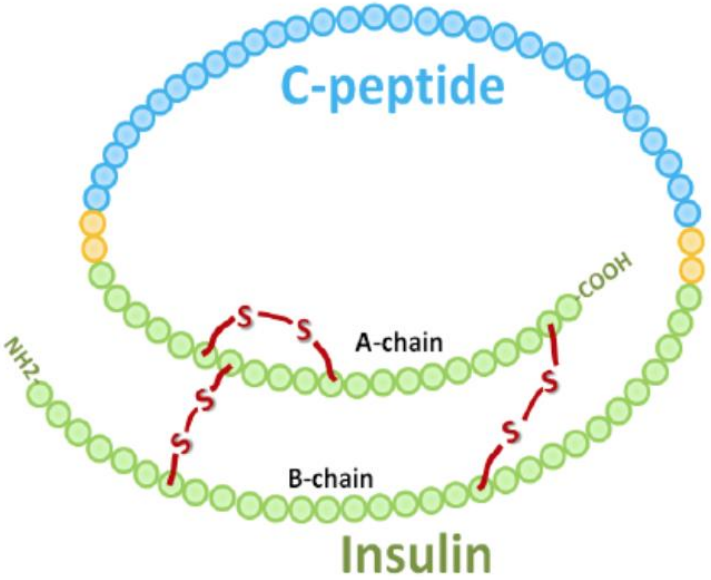

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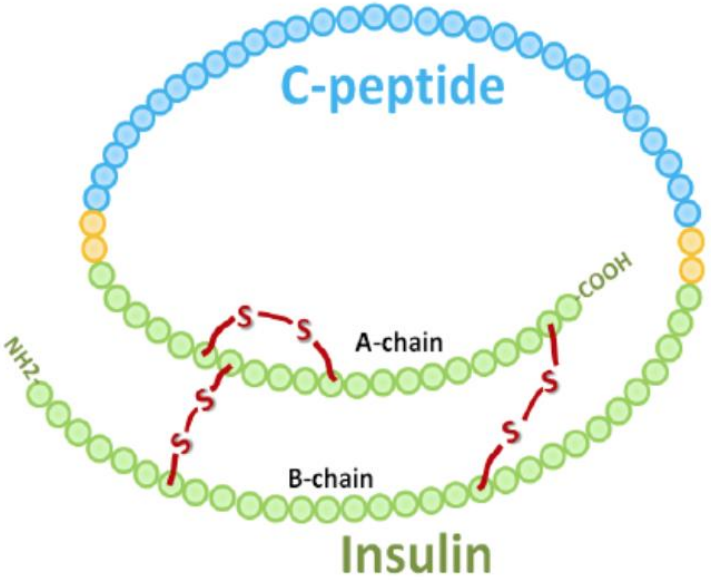

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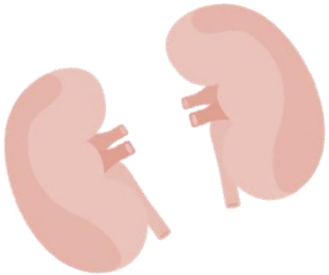
Other causes

- Kidney function



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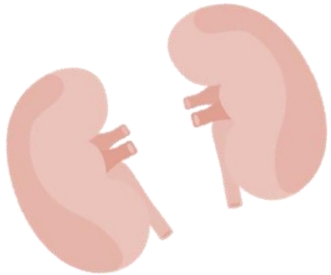
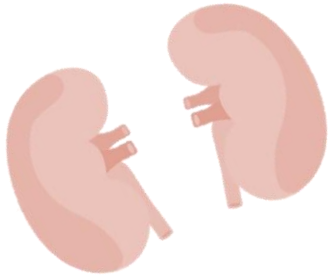


- Diet
- Caloric intake

Other causes

- Kidney function

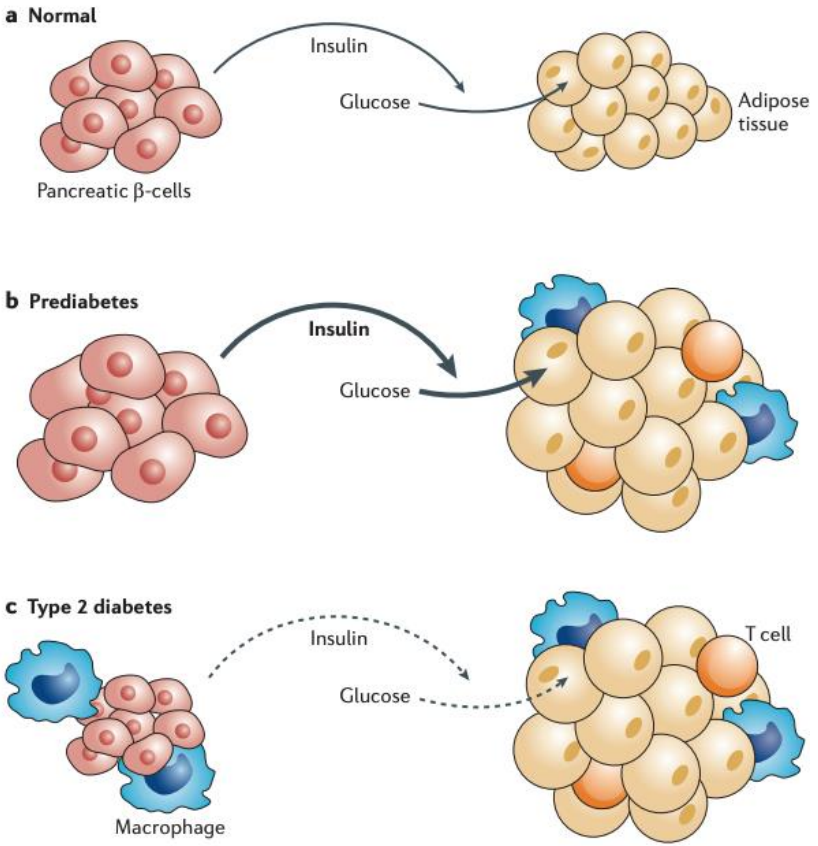


- Diet
- Caloric intake

- Glucotoxicity

Diabetes Mellitus type 2

- Decreased effectiveness of insulin (“insulin resistance”)
- Reduction in beta cell mass and beta cell function



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Inflammation in Diabetes

- Islet inflammation
- Islet amyloid polypeptide

Inflammation in Diabetes

- **Islet inflammation**

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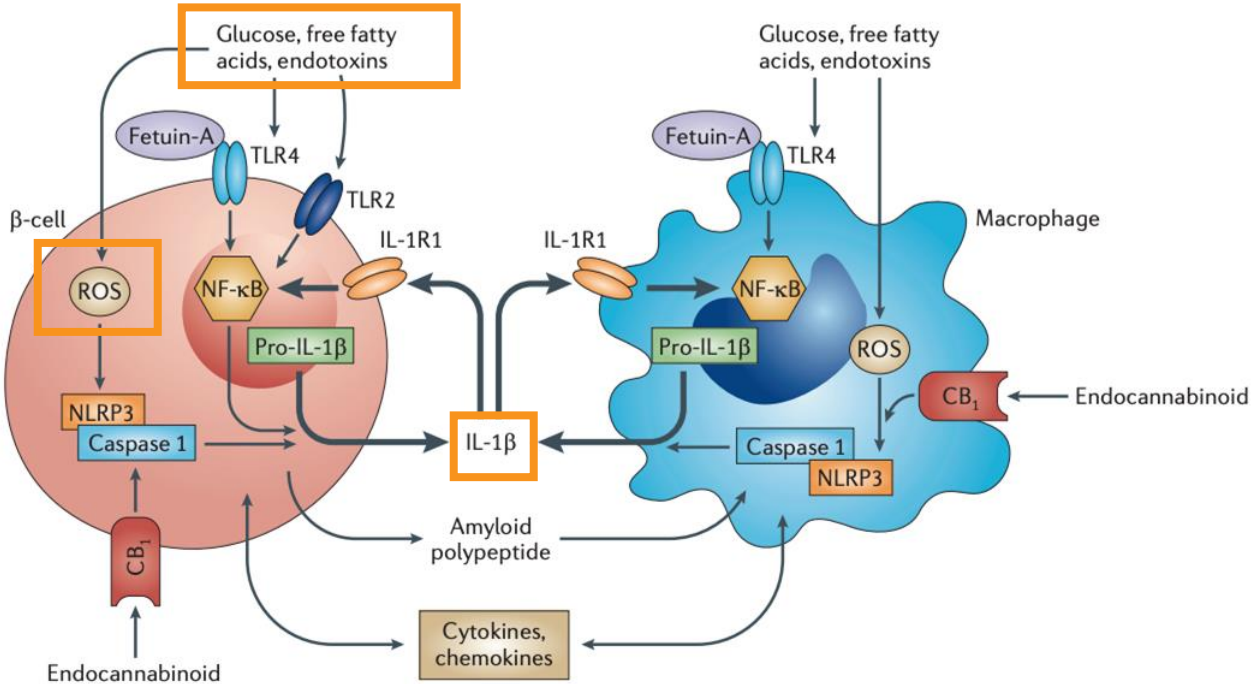
Islet inflammation



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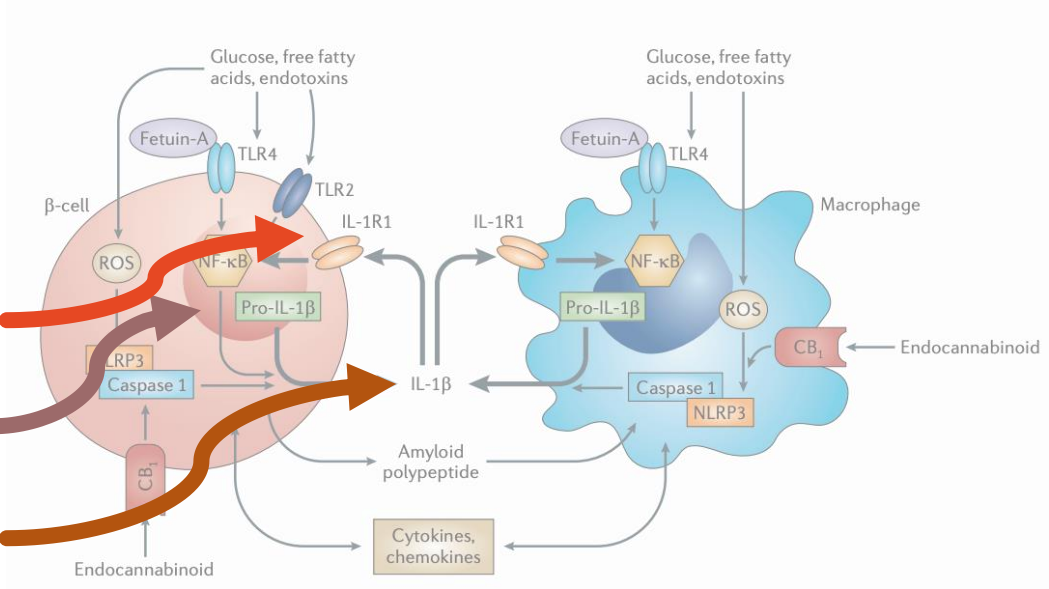
Therapies

- Metformin
- Sulfonylureas (glibenclamide)
- Anakinra (IL-1 receptor blockade)
- Salsalate (IKKβ–NF-κB inhibition)
- Canakinumab (IL-1β antagonism)



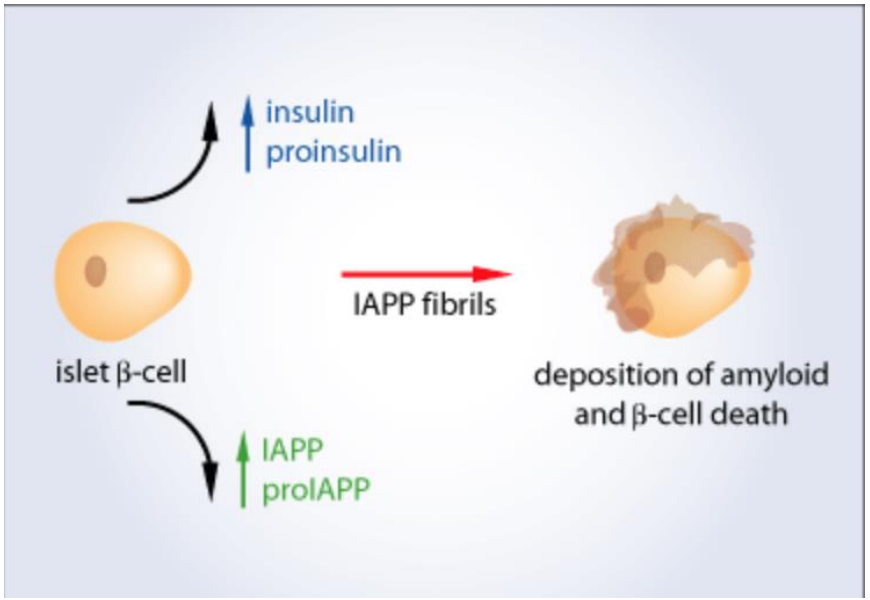
Inflammation in Diabetes

- Islet inflammation

- **Islet amyloid polypeptide**

Islet Amyloid PolyPeptide (IAPP) and DM2

- Islet amyloid polypeptide (IAPP): made in pancreatic beta cells, co-secreted with insulin
- Islet amyloid: aggregation of IAPP
- Aggregation of IAPP fibrils plays a role in beta-cell death and the progression of type 2 diabetes



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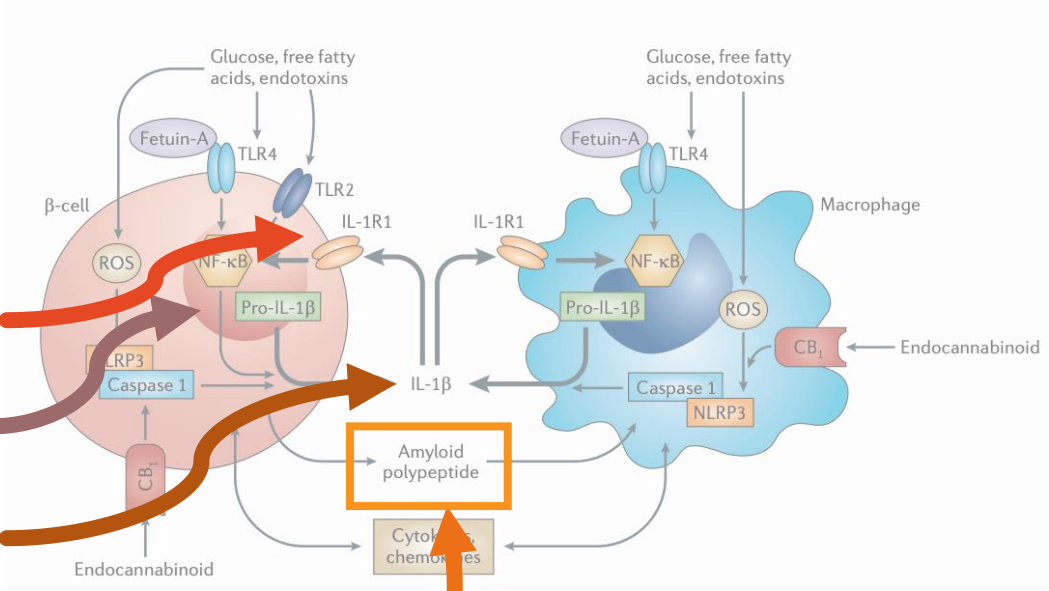
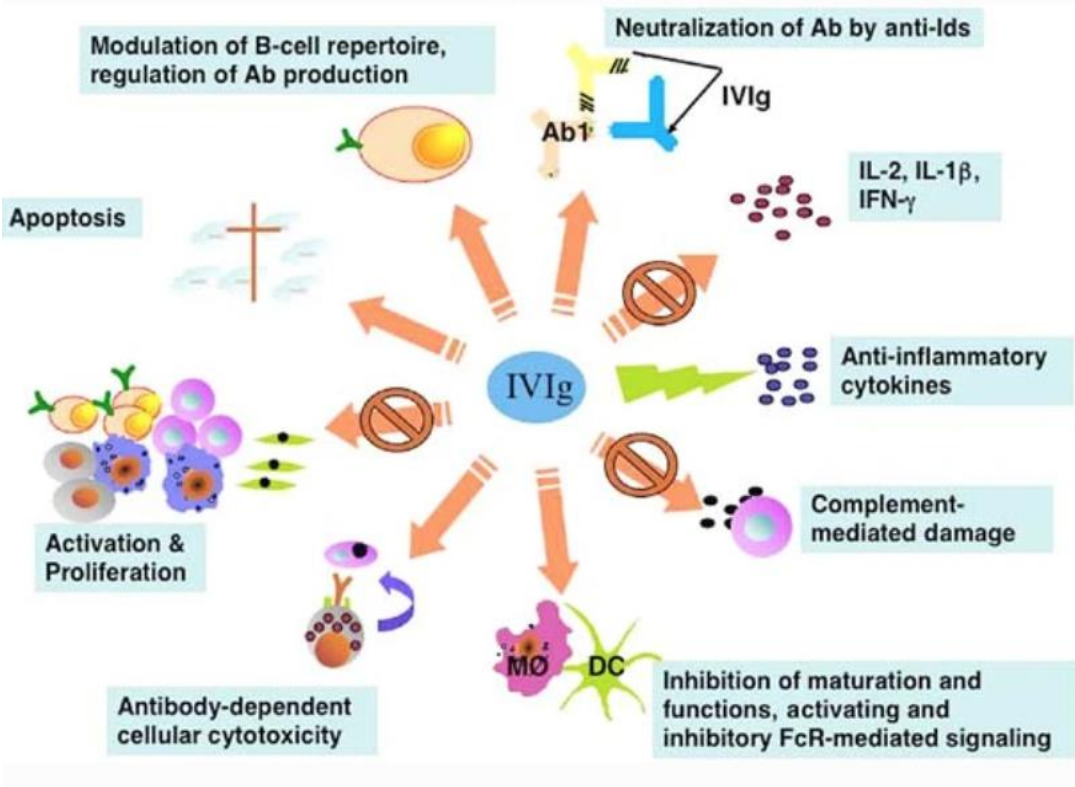
- **Islet amyloid inhibitors**



What about IVIg?



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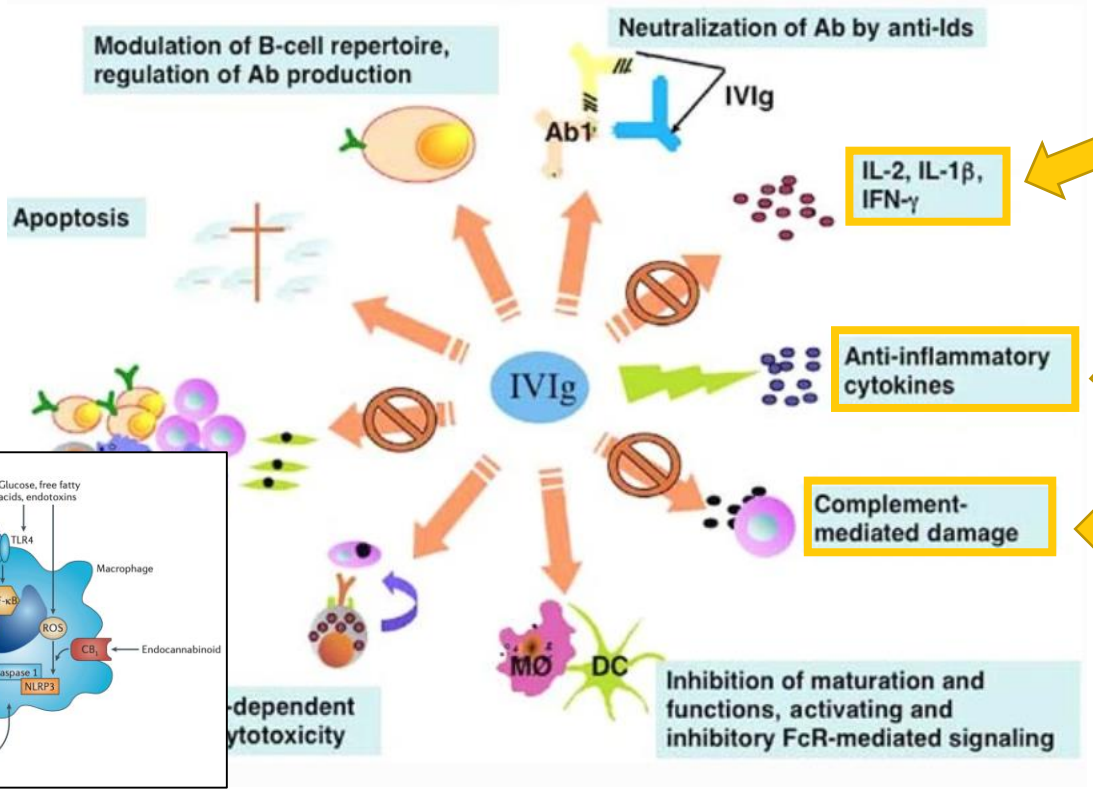

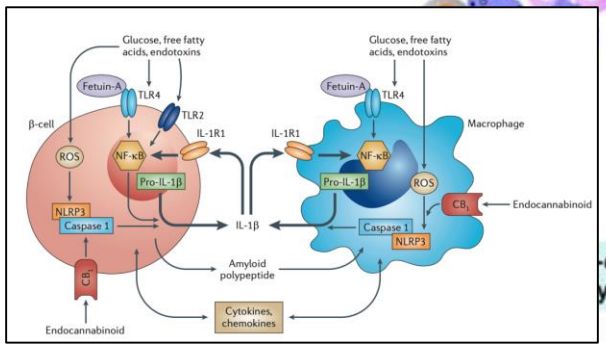

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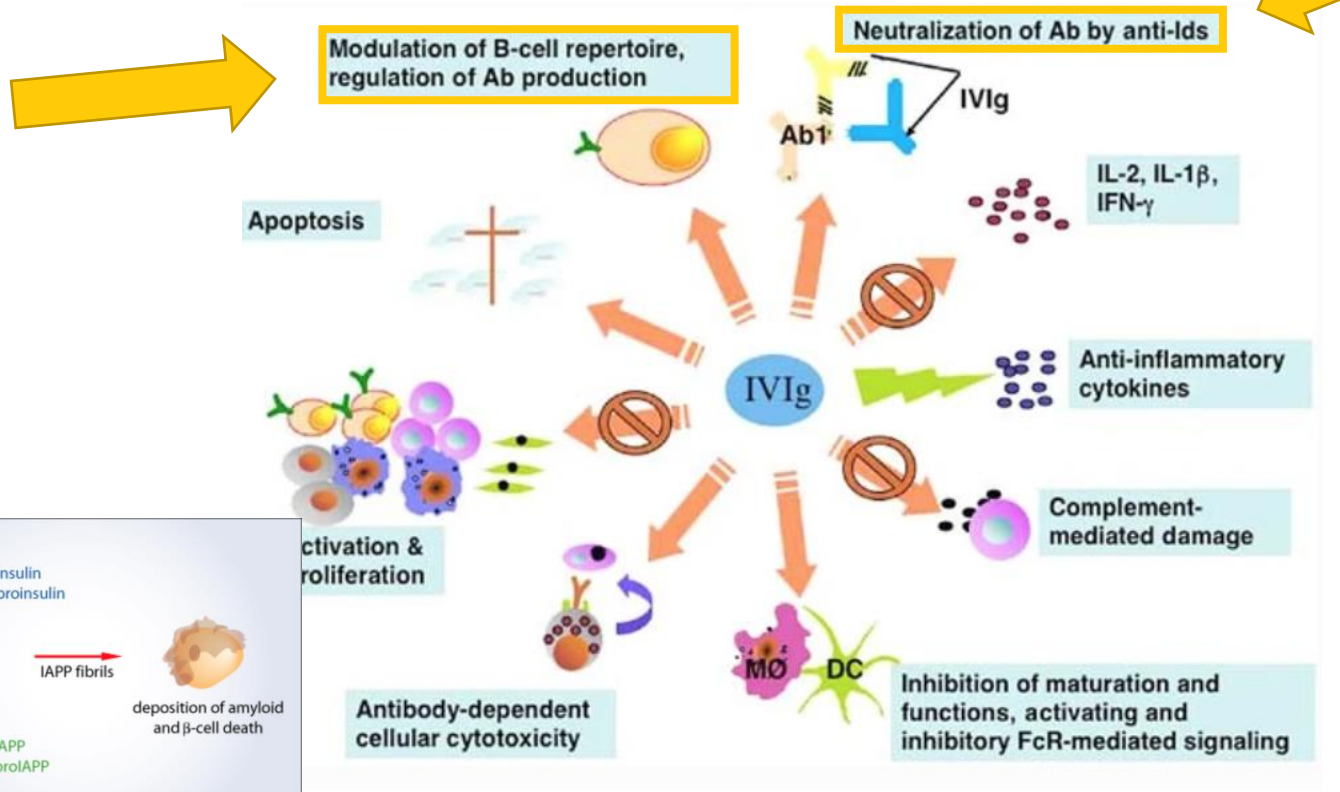

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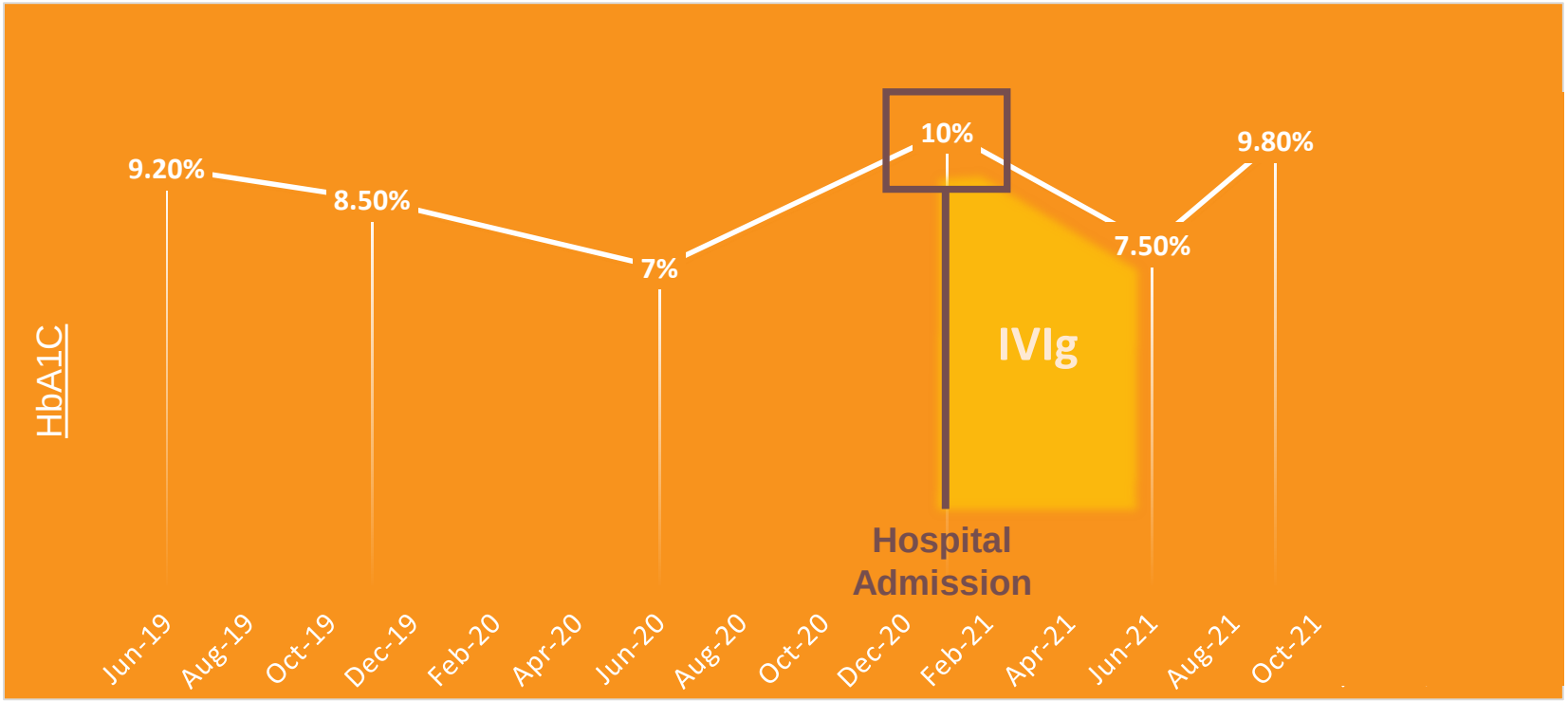
Back to our patient



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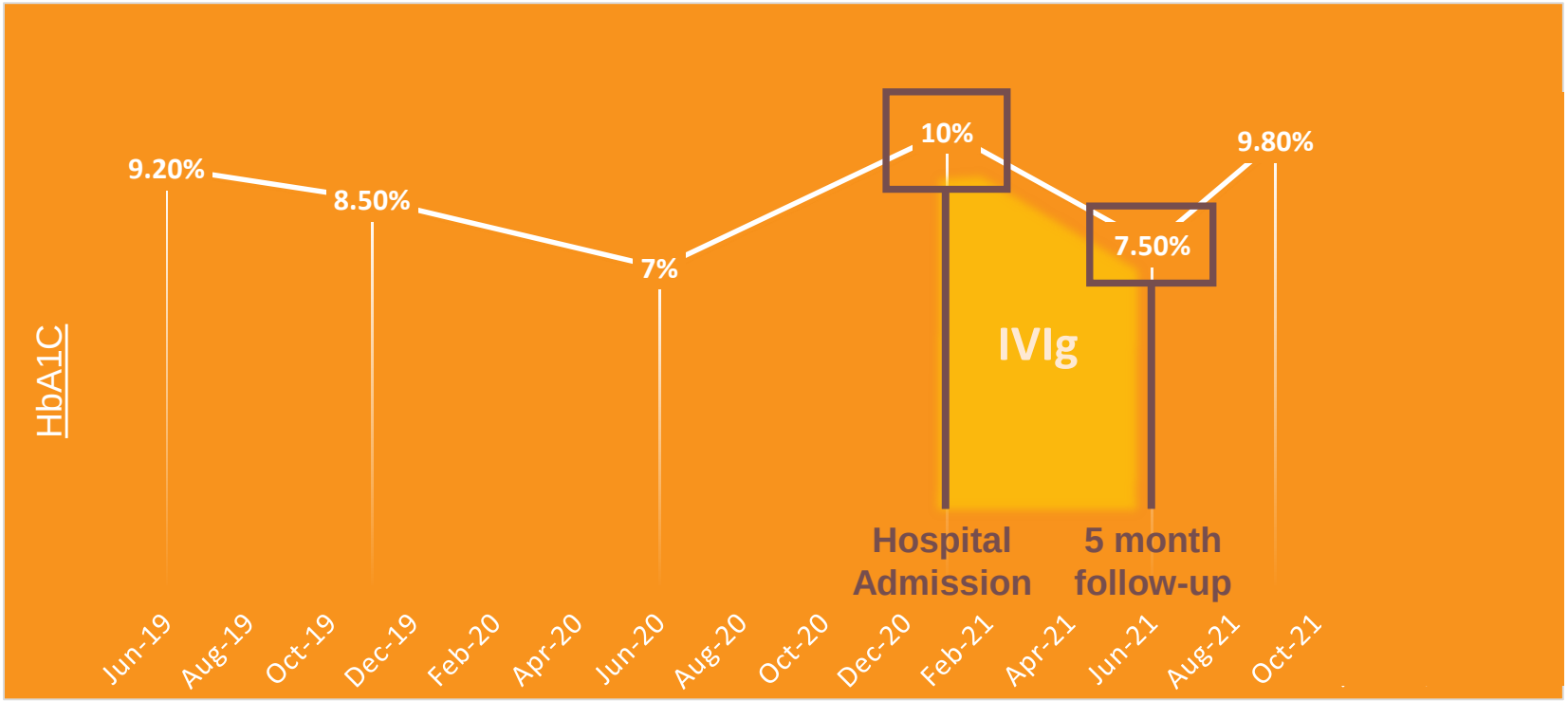

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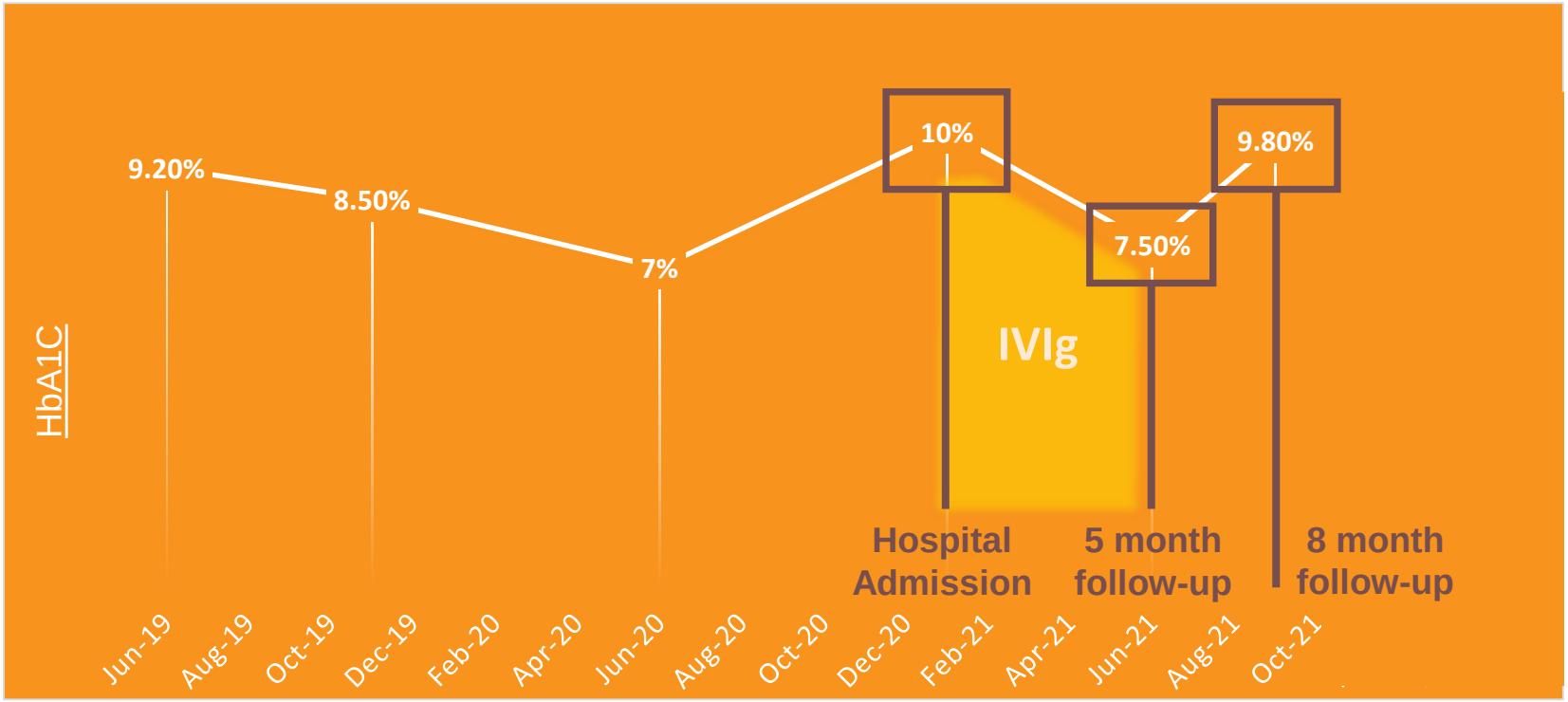
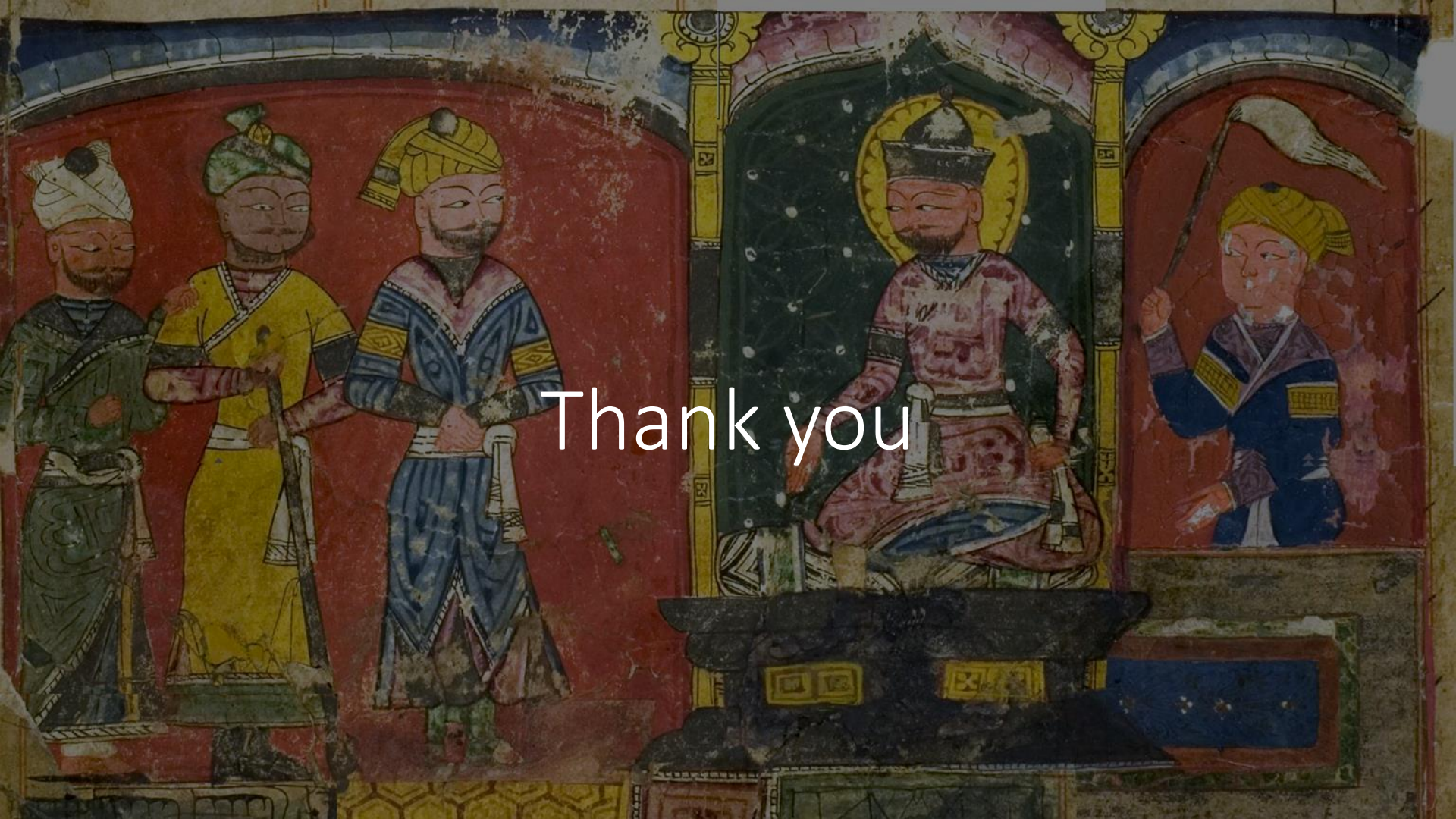


Future role of IVIg in DM2?

- Transient (5 mo) reduction in insulin requirements after treatment with IVIg
- Unique case, first documented of its kind
- Need for further research targeting inflammation in DM2 and insulin resistance

Lessons

- Be studious
- Be curious
- Be open to serendipitous findings


Thank you

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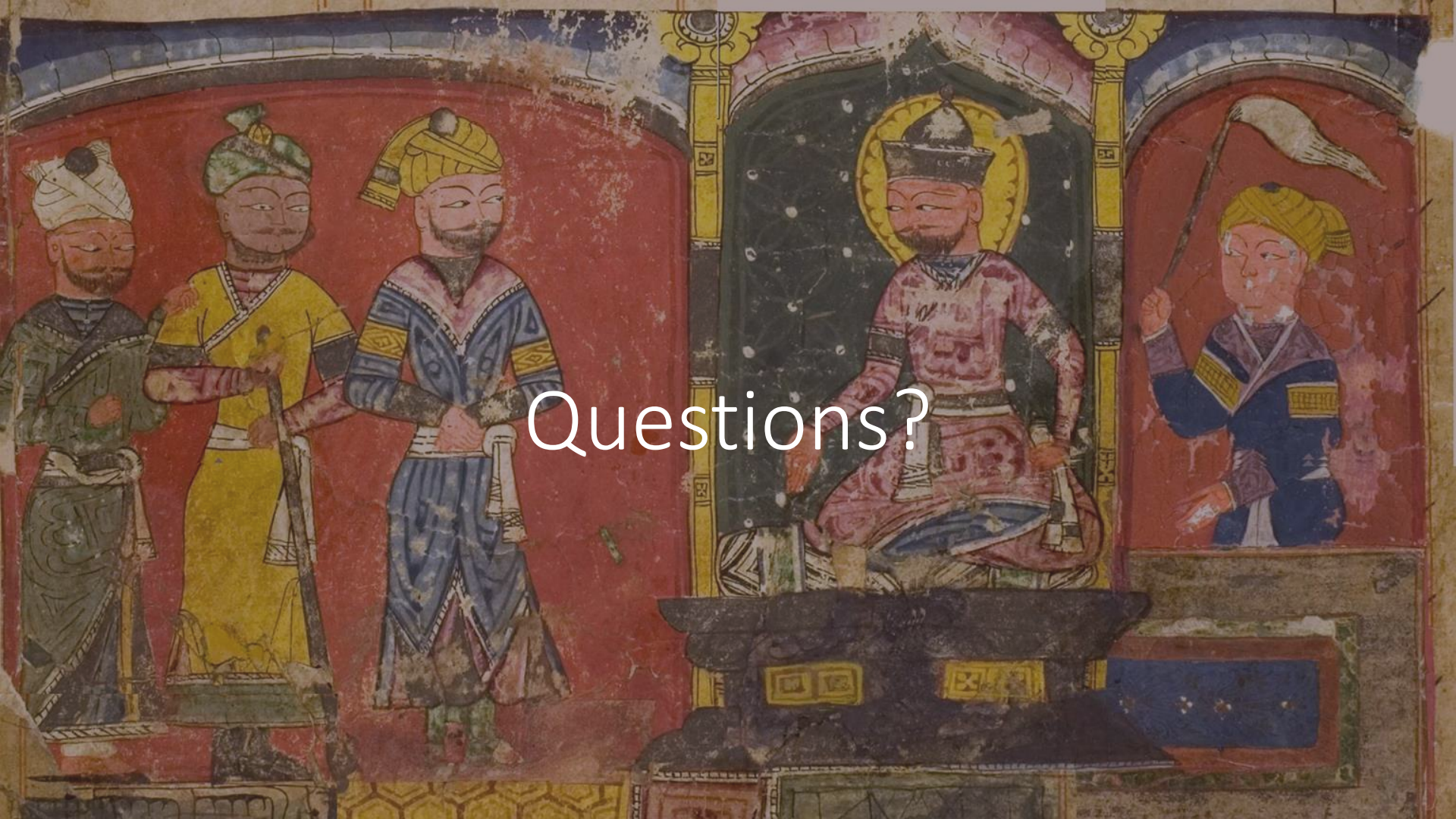
Questions?