

North Carolina Society of Gastroenterology 2024 Annual Meeting



The New IBS Masqueraders

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Joint Providership



American Society for
Gastrointestinal Endoscopy

Disclosures:

Research Support: Revivacor, EvoEndo

Principle Investigator of Trials: Exact Sciences,
Guardant Health, Clinical Genomics, Polymedco, Finch
Therapeutics (ended), Freenome Holdings (ended)

Investments: Seattle Genetics, Abbott Labs

Patents: Artificial intelligence in colonoscopy

Objectives

- understand two recently-described conditions that can cause diarrheal IBS symptoms: Alpha-gal syndrome and sucrase-isomaltase deficiency
- understand the diagnosis and management of both conditions and limits to knowledge

Case: 58- year-old woman with 2 months of bloating, urgency and diarrhea



- healthy prior
- no relationship to particular foods
- celiac titers normal
- serum IgE to alpha-gal 1.27 U/L (elevated ULN <0.1 U/L)
- improvement on alpha-gal free diet
- reexposures reproduced symptoms

McGill et al. *Am J Gastro* June 2022

Alpha-gal syndrome== a delayed allergic reaction to a sugar present in all lower mammals and products derived from them



Alpha-gal Syndrome Symptoms

2-6 hours after ingestion:



Abdominal pain,
diarrhea, nausea,
vomiting



Hives, urticaria, angioedema

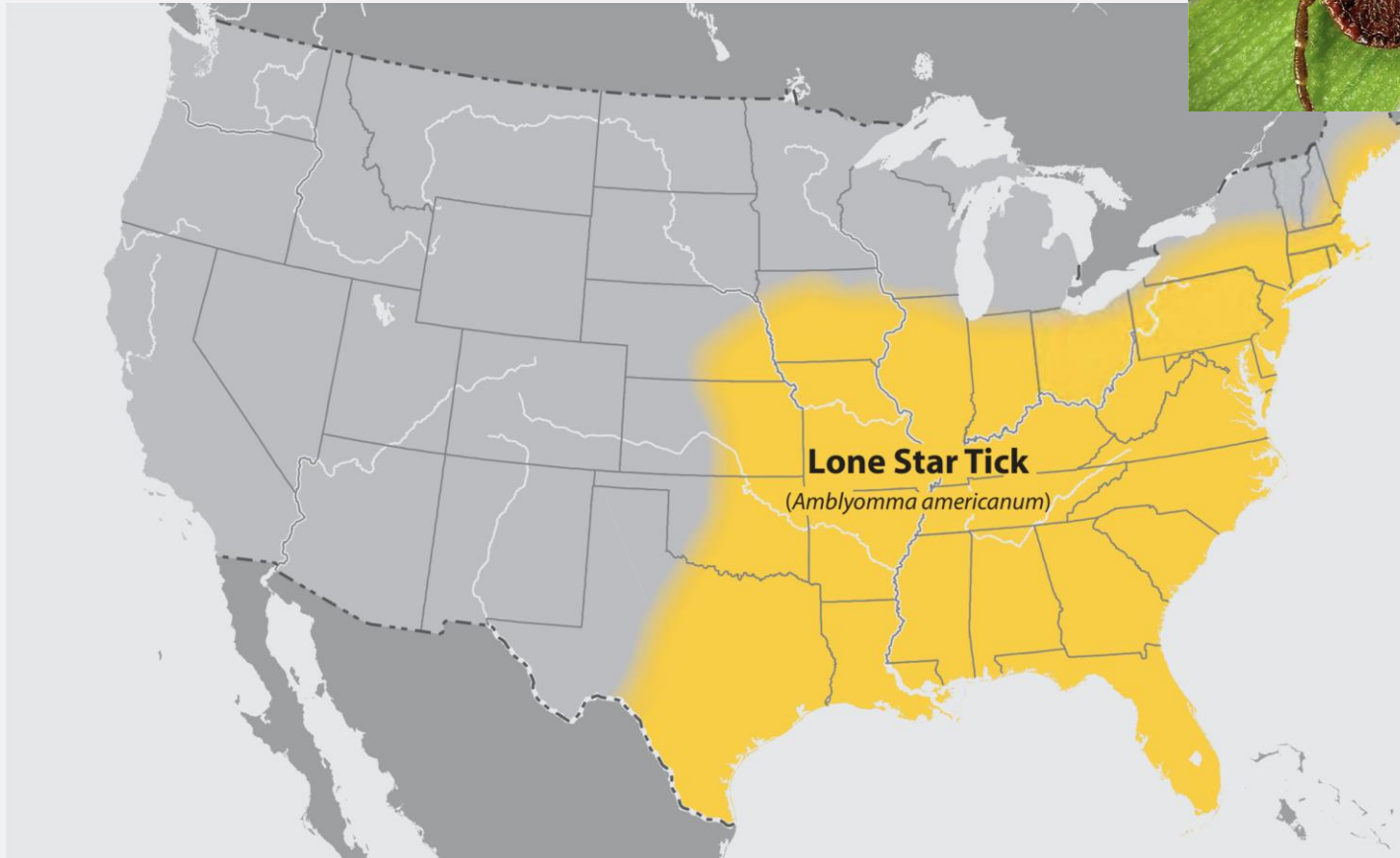
Anaphylaxis

Gastrointestinal Alpha-gal Syndrome : Predominant or Isolated GI Symptoms



=Recurrent abdominal pain, diarrhea, nausea, vomiting
+ alpha-gal IgE elevated
+ symptom relief on alpha-gal avoidant diet

Alpha-gal Syndrome Prevalence Region





DIAGNOSIS



Patients with unexplained abdominal pain, diarrhea, vomiting, particularly:

- from alpha-gal prevalent region
- activities outdoors
- symptoms after eating red meat
- symptoms awaken patient from sleep

Alpha-gal IgE elevated

- alpha-gal- avoidant diet
- tick bite prevention

2 month follow-up

Adequate symptom relief:

- continue alpha-gal avoidant diet
- consider liberalizing to eat dairy, gelatin
- follow-up in 12 months, recheck alpha-gal IgE

Alpha-gal IgE negative

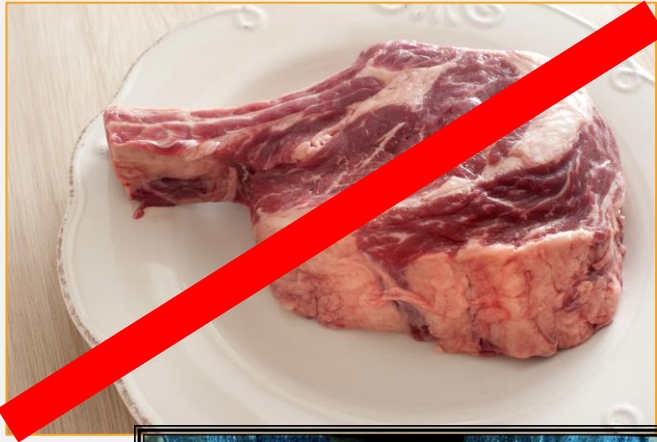
continue diagnosis + management

No or minimal symptom relief:

- consider other diagnoses and management

McGill, Al Hashash, Platts-Mills. *Clinical Gastro Hep* 2023

Alpha-gal Syndrome Management: Avoid the Allergen and further tick bites



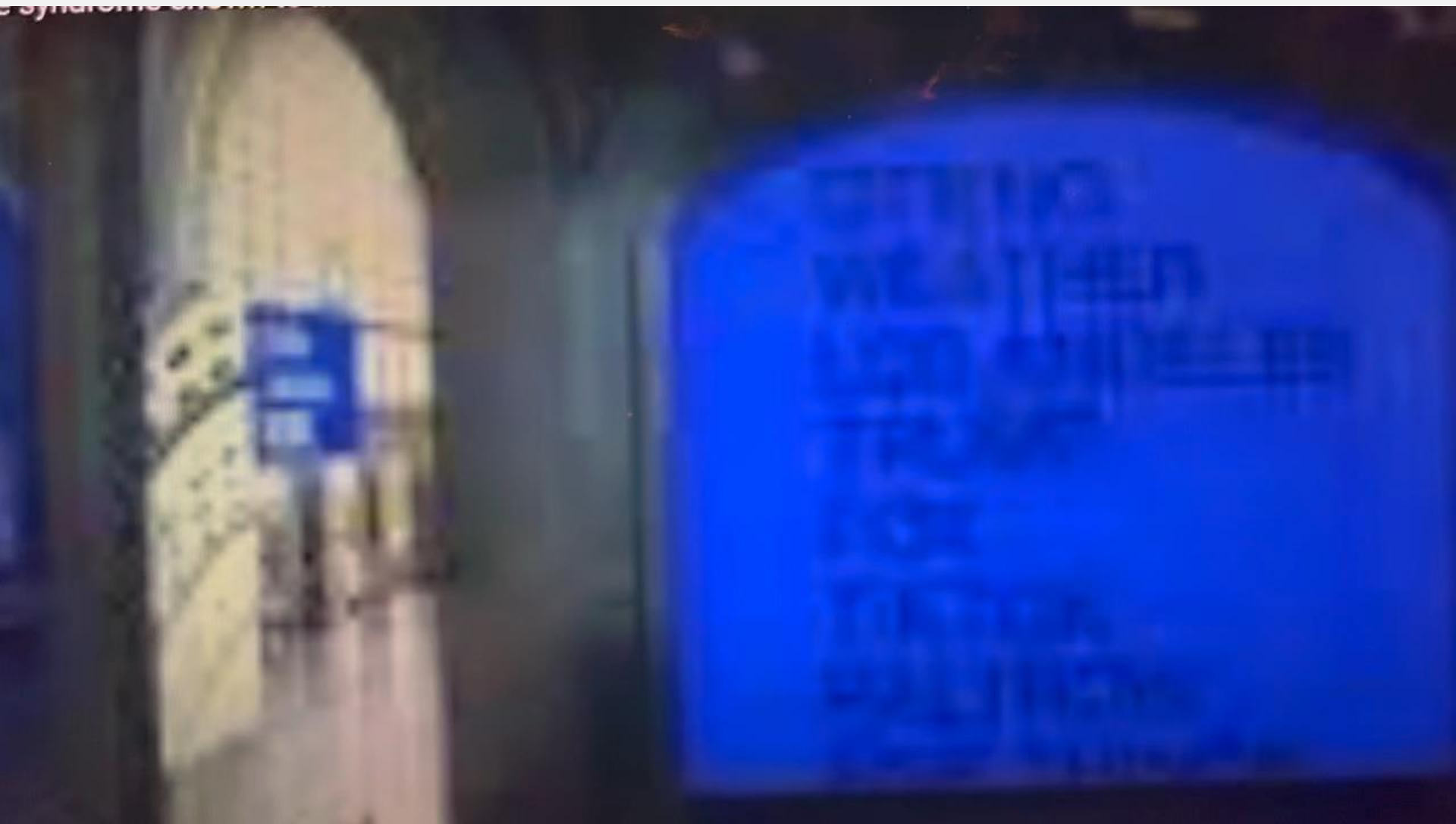
antihistamine



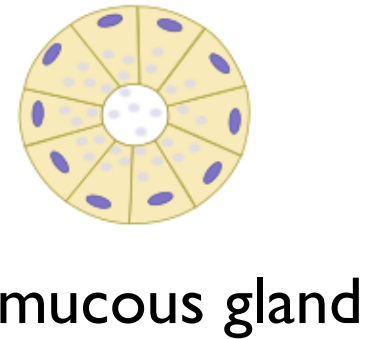
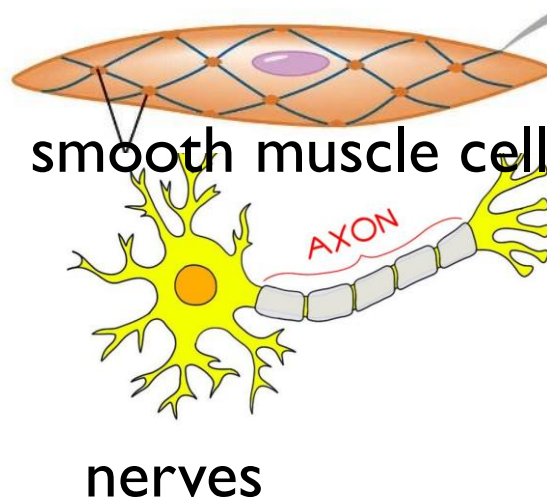
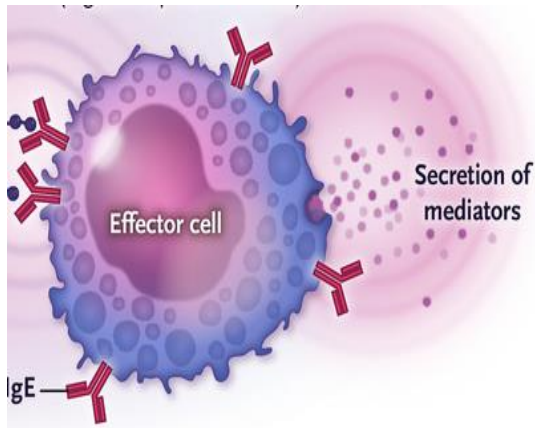
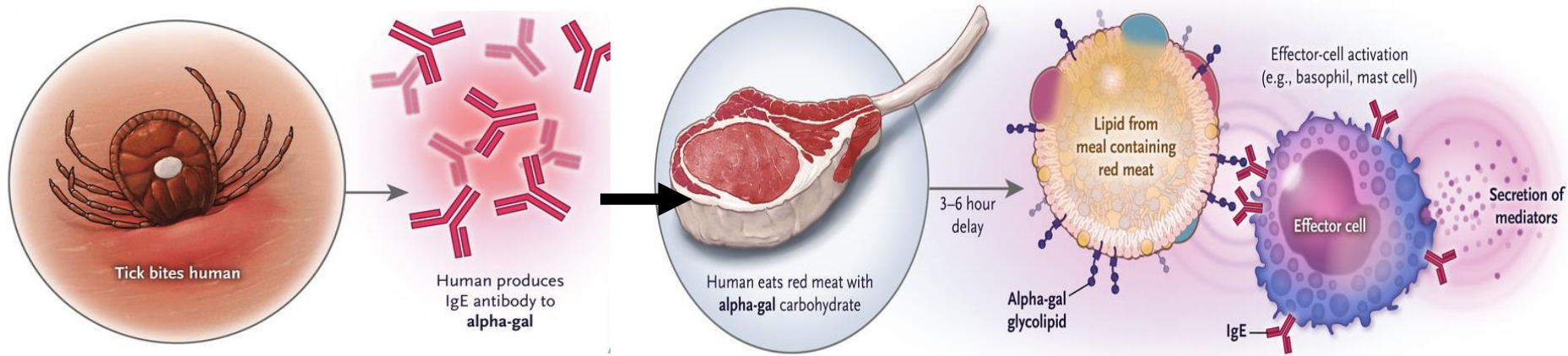
Epinephrine
autoinjector for
systemic
symptoms



... syndrome...



Alpha-gal Syndrome Pathophysiology



Houchens et al. *NEJM* 2021

Isolated Gastrointestinal Alpha-gal Meat Allergy Is a Cause for Gastrointestinal Distress Without Anaphylaxis

16 GI Clinic Patients with Abdominal pain, Diarrhea, nausea, vomiting all with follow-up (median 1 yr)



Median alpha-gal
IgE = 0.61
range 0.26-100
IU/L



75% recalled
a tick bite

Symptom Improvement on alpha-gal avoidant diet



resolution n=4



significant improvement

n=8



some n=4

Croglio, Commins, McGill. *Gastro* 2021

**BE HONEST.
IS THIS TOO MUCH**



LETTUCE?



Case: 23 year-old man with abdominal pain, bloating and diarrhea



- symptoms since childhood
- Celiac, IBD testing negative
- On duodenal biopsies:

Enzyme activity	% of normal
Sucrase	15%
Maltase	25%

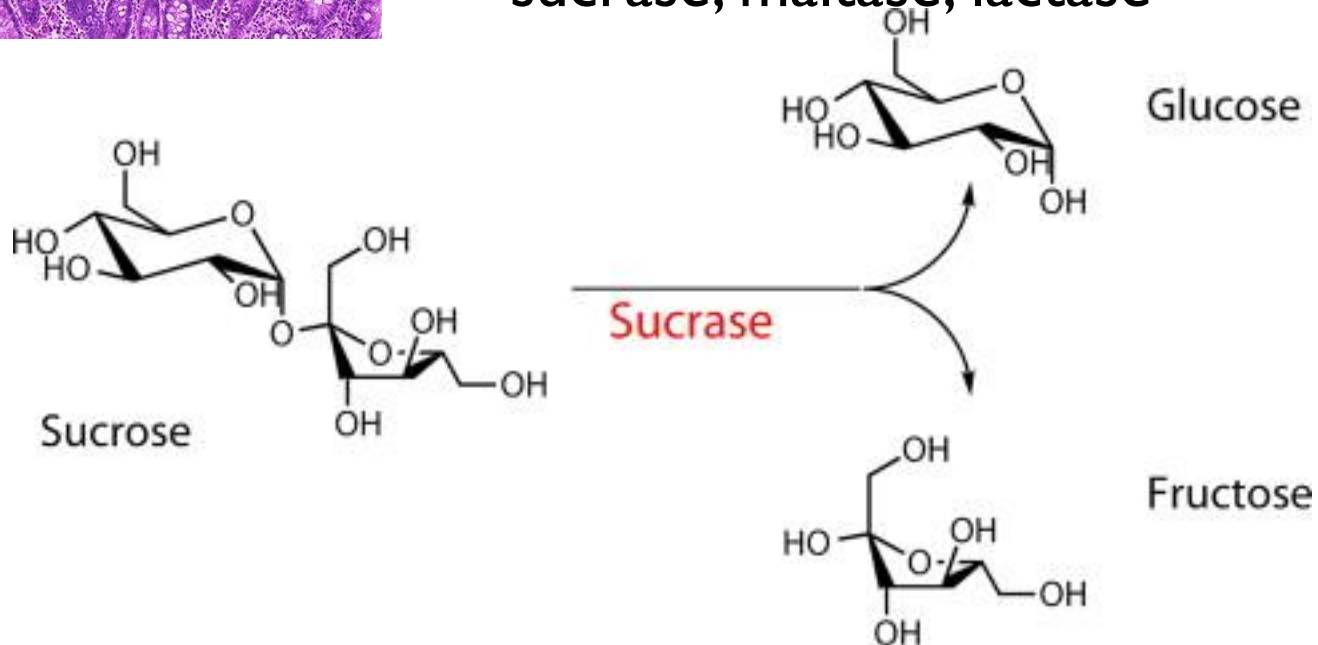
- improvement on low sucrose diet + sacrosidase

Foley et al. *Gut* June 2022

Sucrase-Isomaltase deficiency: “A thing” in adult GI?



- enzymes at the brush border help us break down disaccharides into monosaccharides
- sucrase, maltase, lactase



Sucrase-Isomaltase deficiency

Congenital

- autosomal recessive
- various genetic variants
- prevalence: 0.2% in North America, 10% in Greenland eskimos
- heterozygotes may be predisposed to IBS

Viswanathan and Rao. *Curr Gastro Reports* 2023
Henstrom et al. *Gut* 2018

Acquired

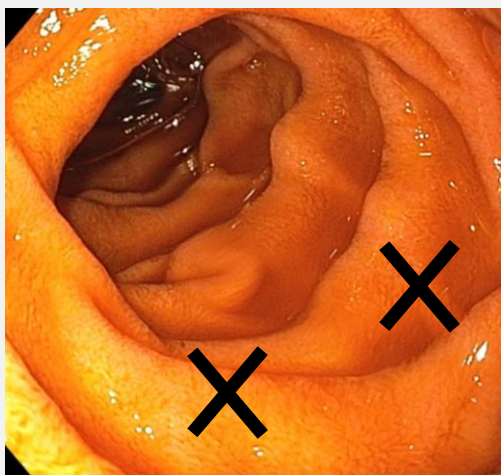
- pigs experimentally infected with diarrheal virus have low disaccharidase levels
- Potential causes: infections, celiac disease, Crohn's, immunodeficiency, SIBO, others??

Helm et al. *PLOS ONE* 2020
Helm et al. *PLOS ONE* 2020

Sucrase-Isomaltase deficiency: Retrospective studies in Adults with IBS- diarrhea, bloating, nausea and duodenal bxs

Author	Place	#	% with sucrase-isomaltase deficiency	Symptom improvement on follow-up
Kim et al 2019 <i>Dig Dis Sci</i>	Miami	31 adults	35% (n=11)	Not given
Viswanathan 2020 <i>J Neuro Mot</i>	Augusta	120	10% (n=12)	Not given

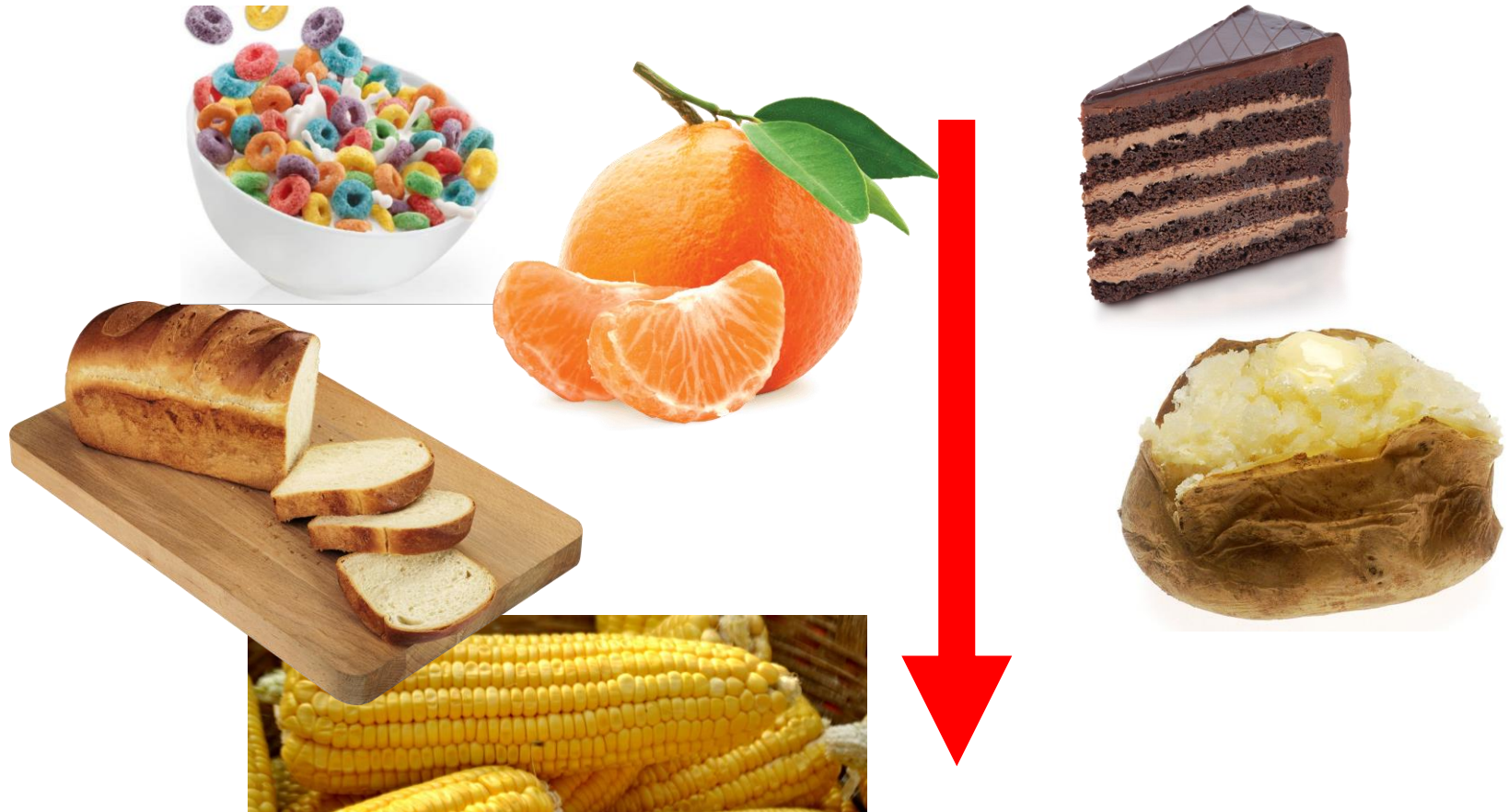
Diagnosis: 2 duodenal biopsies sent in sterile jar for “disaccharidase testing”



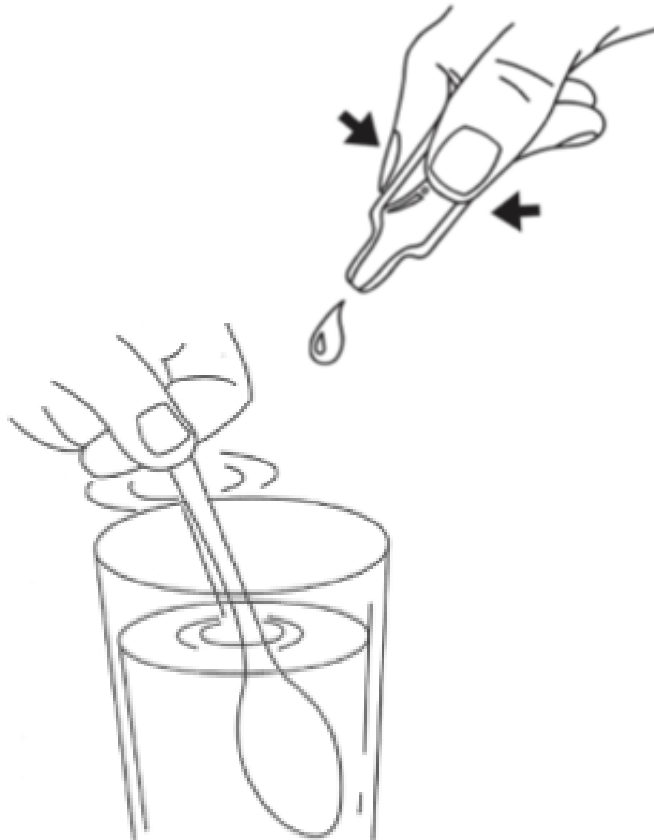
Enzyme	Activity
Lactase	1.9 (!) LOW
Sucrase	59
Maltase	153

- 2 biopsies of 2nd portion duodenum
- sterile jar, NO formalin, gauze or media; on ICE ship frozen
- results: disaccharidase activity vs normal

Management: low sugar/ starch diet



Management: + sacrosidase with meals



- 2mL with meals improved symptoms and diet in 28 kids with congenital deficiency
- FDA-approved for congenital
- specialty pharmacy
- must be refrigerated
- mix with room-temperature water or milk

Conclusions

- Alpha-gal syndrome causes a delayed allergic reaction (hours) to mammalian meat and products
- Symptoms may only be GI distress, and diagnosis is with elevated serum IgE to alpha-gal and improvement of symptoms on avoidant diet
- no double-blind challenge to date

- Sucrase-isomaltase deficiency causes bloating, diarrhea and nausea and may be congenital or acquired
- treatment is low sugar/starch diet and sacrosidase with meals
- no follow-up info on adults w/ acquired, to date

CME/MOC Question:

You see a 34-year old man in your clinic who has awakened from sleep with vomiting and abdominal pain on three occasions, the last after eating a steak dinner. How do you screen for alpha-gal syndrome?

- a) serum IgE to alpha-gal
- b) allergy skin test
- c) blood galactosemia
- d) IgG to alpha-gal

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CME/MOC Question:

You see a 34-year old man in your clinic who has awakened from sleep with vomiting and abdominal pain on three occasions, the last after eating a steak dinner. How do you test for alpha-gal syndrome?

- a) serum IgE to alpha-gal
- b) allergy skin test
- c) galactosemia reflex, blood
- d) IgG to alpha-gal

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Thank you!
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Symptomatic: A Medical Mystery Podcast
Case #12: Chris



SYMPTOMATIC

00:00 32:05

Case #12: Chris

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