



The Childrens Allergy

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Histamine Intolerance & Mast Cell
Activation Syndrome (MCAS)

Clinical Considerations and the Role of Dietitians

British Dietetic Association

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**Histamine
intolerance:
overview and
clinical features**

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**MCAS: what it is
and how it presents**

03

**Diagnostic
challenges**

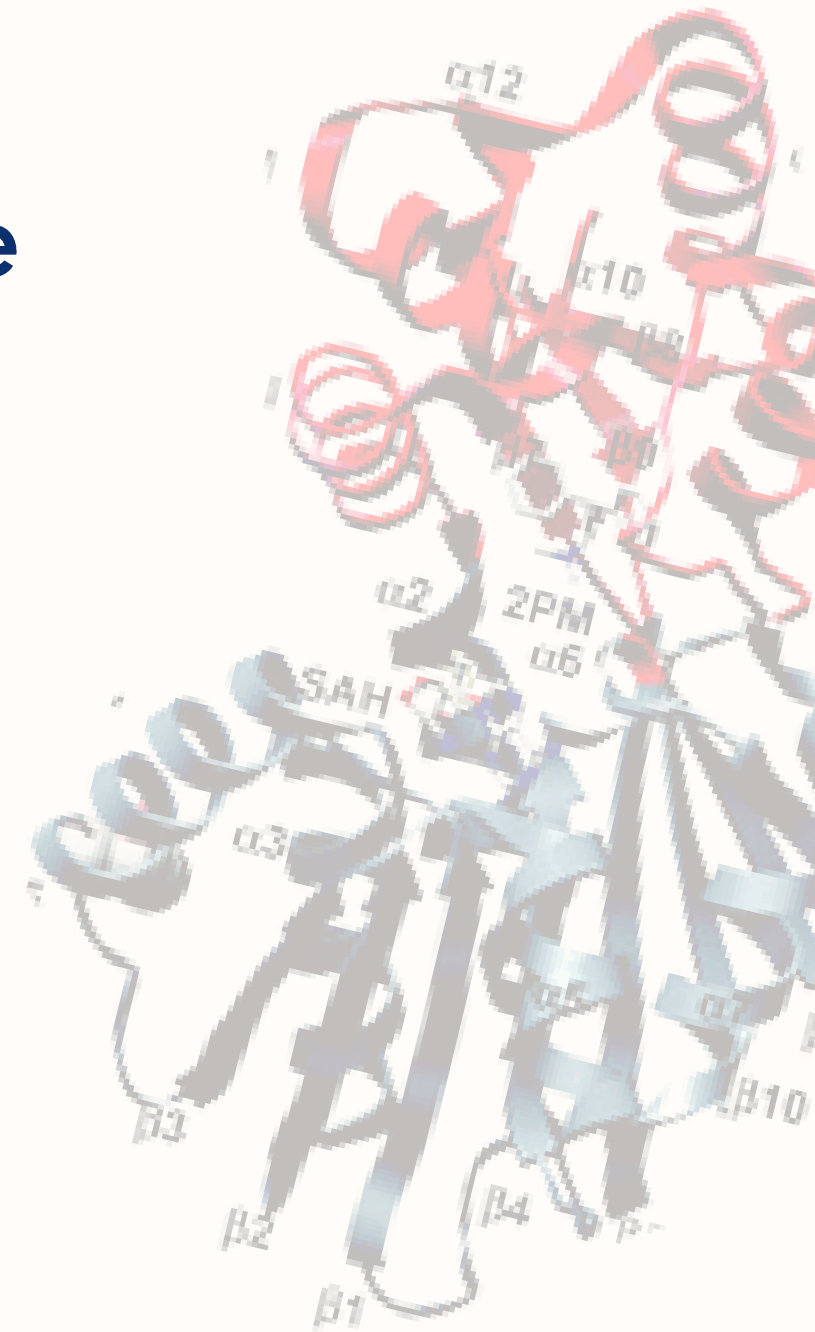
04

**Management
approaches and the
role of dietitians in
supporting patients**

Histamine Intolerance

What Is It?

- Non-IgE-mediated reaction to excess histamine
- Caused by impaired histamine degradation
- First described over 60 years ago
- Gaining attention since EFSA's 2011 report
- Estimated to affect ~1% of the population
- Often under diagnosed



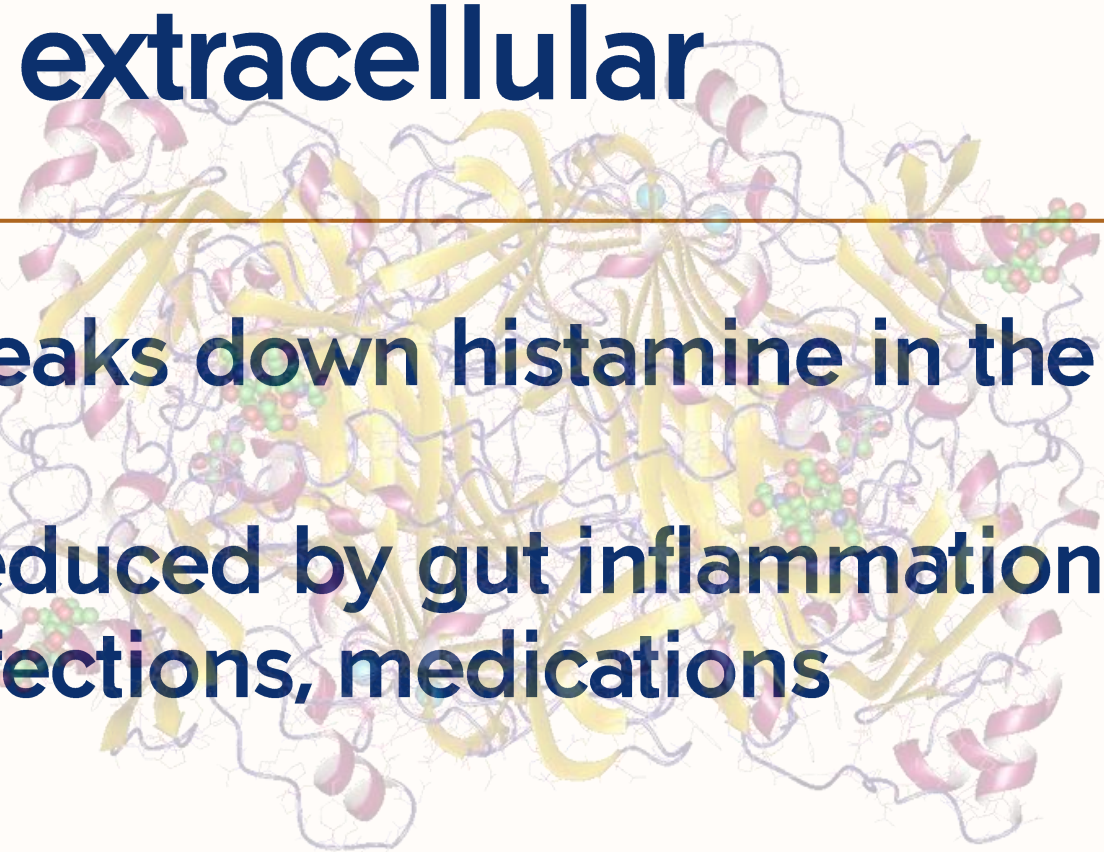
Histamine Metabolism

– Key Enzymes

DAO (Diamine
Oxidase)

is extracellular

- Breaks down histamine in the gut
- Reduced by gut inflammation, infections, medications



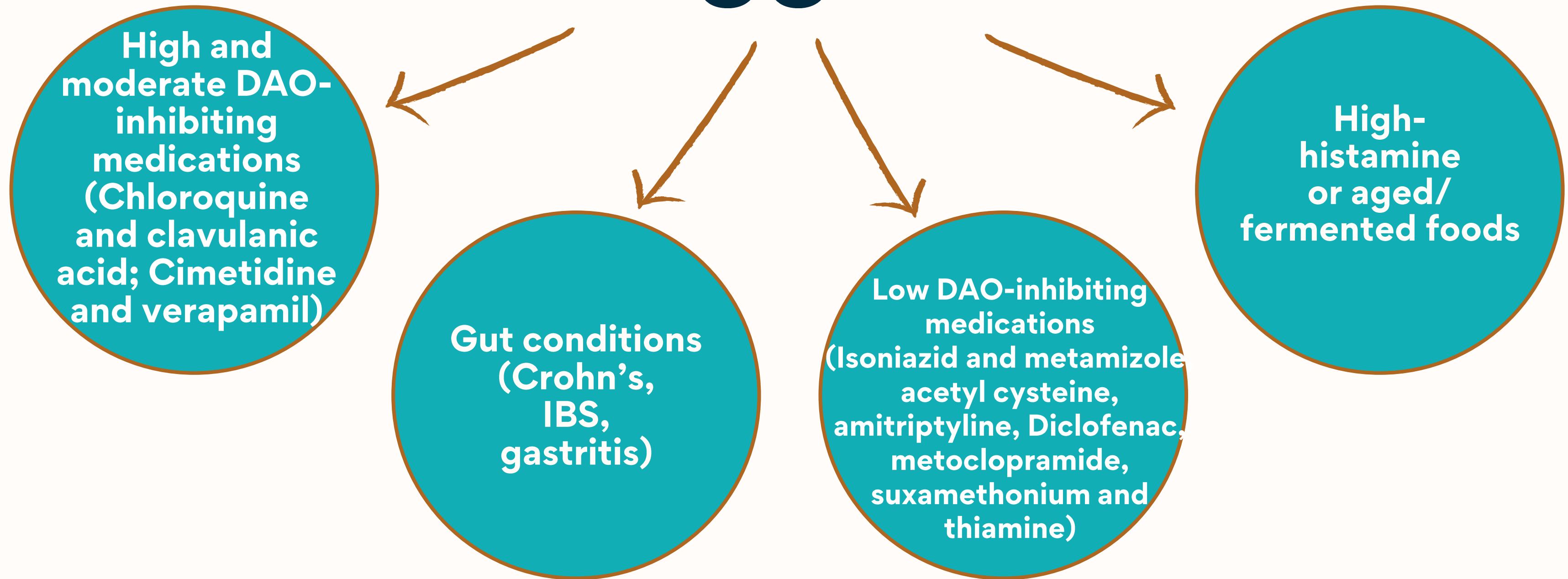
HNMT (Histamine-N-
methyltransferase)
is intracellular

- Breaks down histamine in brain, liver, lungs

- Reference: Maintz L, Novak N. Histamine and histamine intolerance. Am J Clin Nutr. 2007;85(5):1185–96. [PMID: 17490952]

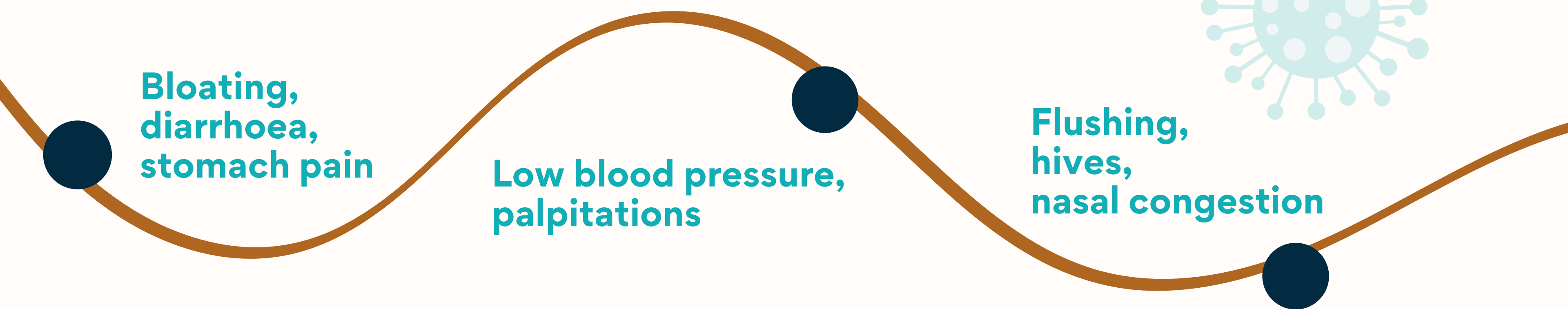


Histamine build-up Triggers



Common Symptoms of Histamine Intolerance

DAO-related:



**Bloating,
diarrhoea,
stomach pain**

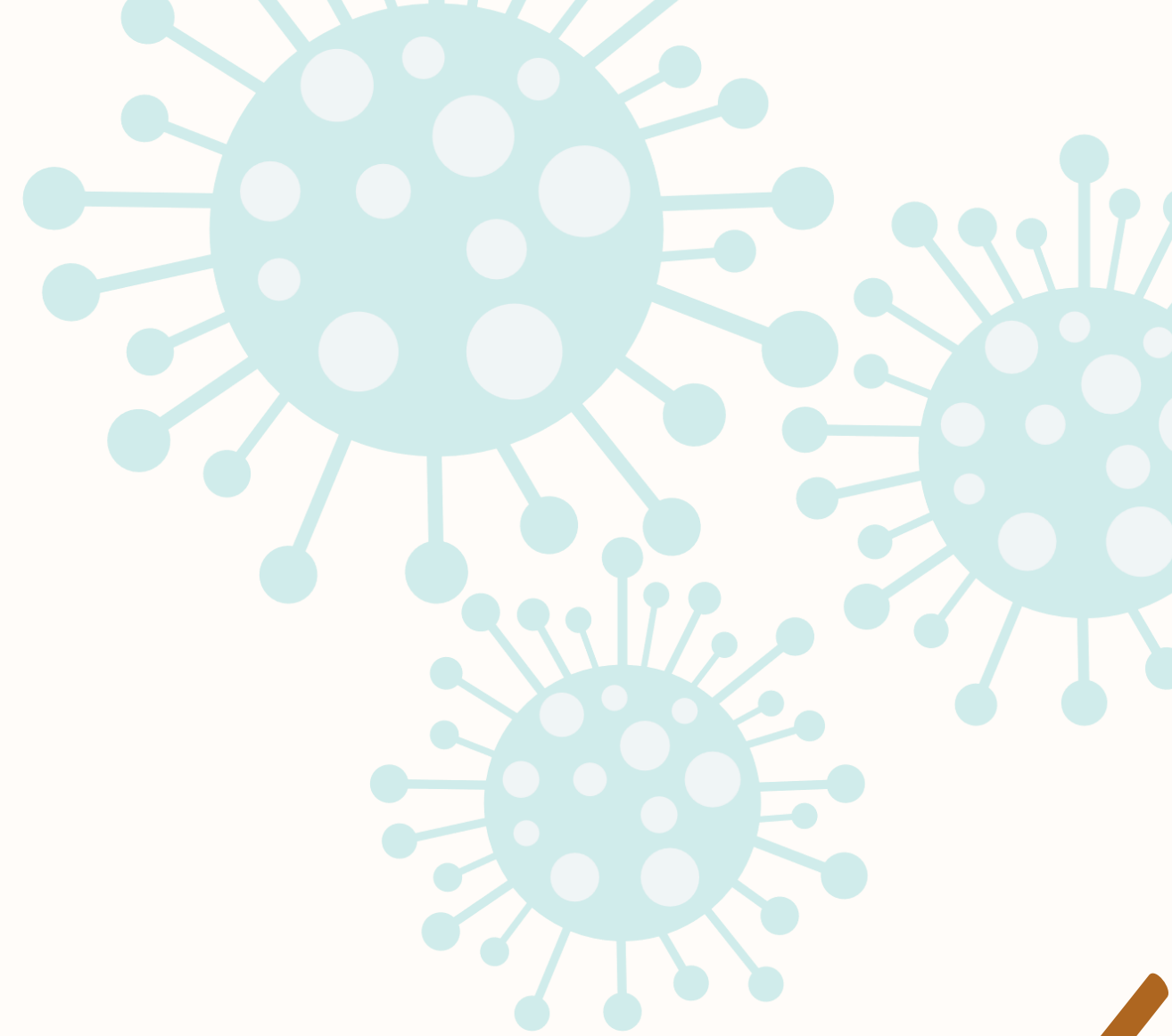
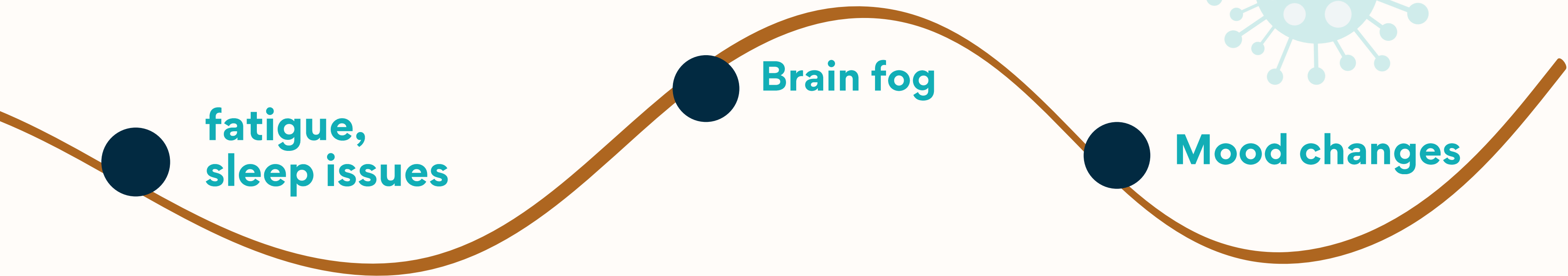
**Low blood pressure,
palpitations**

**Flushing,
hives,
nasal congestion**



Common Symptoms of Histamine Intolerance

HNMT-related:



Severe Symptoms

Scombroid Poisoning

= histamine fish poisoning, **not an allergy**



- Triggered by spoiled fish (e.g. tuna, mackerel, sardines, anchovies)

Abdominal
cramps,
vomiting,
diarrhoea

Bronchospasm,
respiratory distress,
vasodilatory shock (rare
but serious)

Palpitations,
headache, dizziness

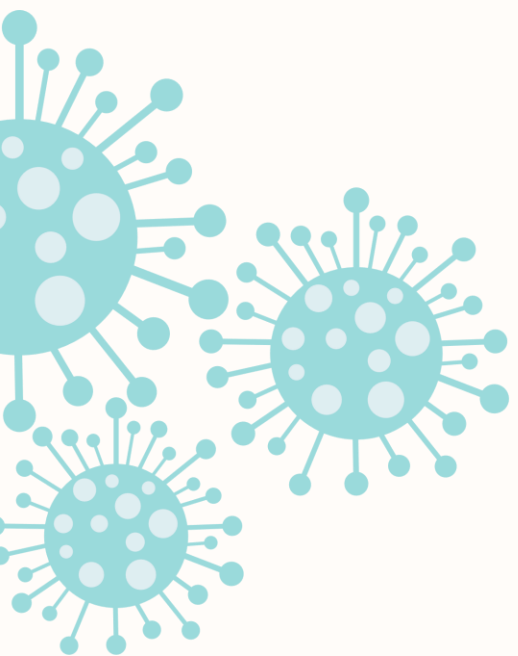
Widespread
flushing
& rash

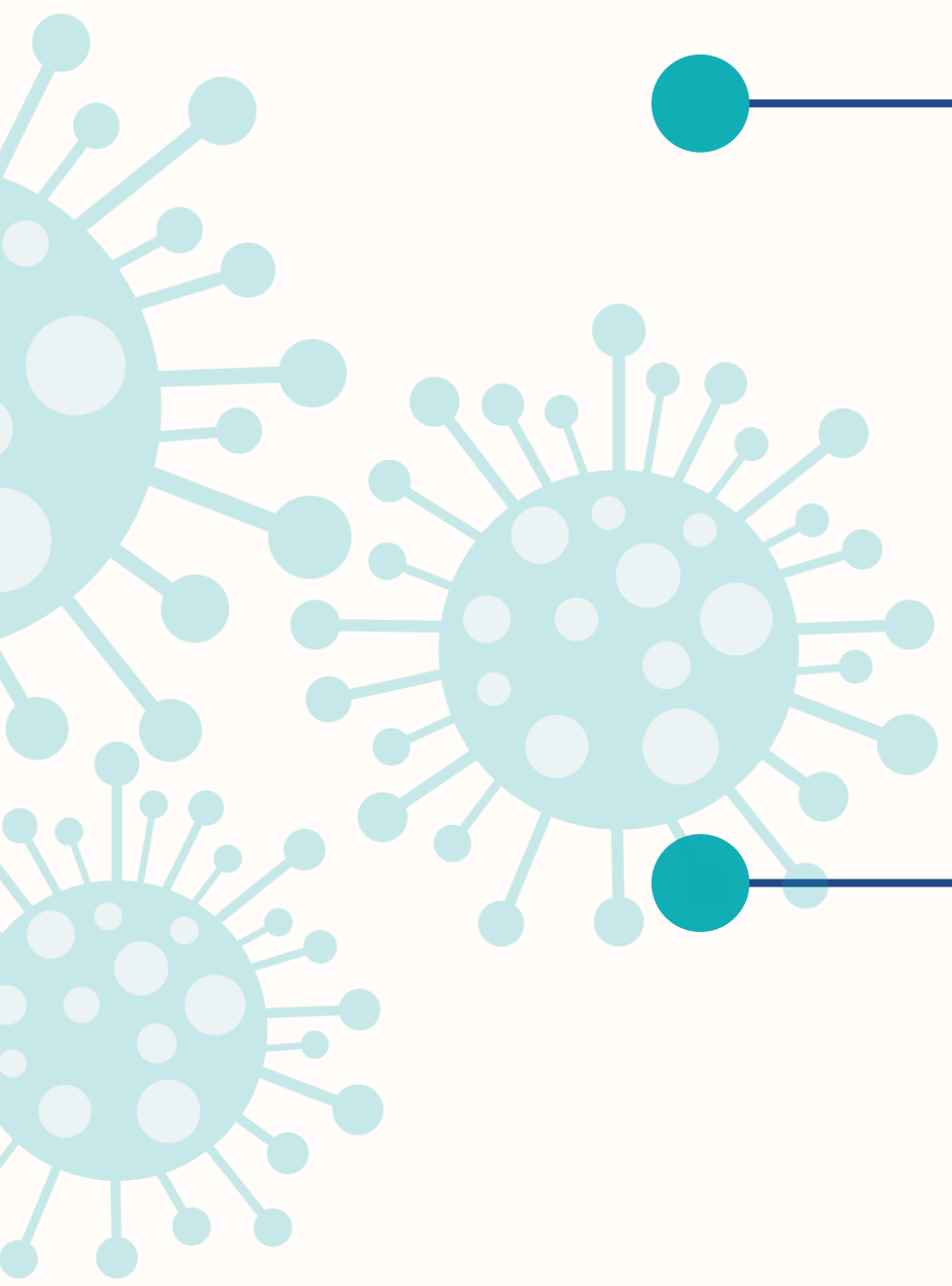
- **Symptoms** usually start within **10-90 minutes** and last hours to a day

Histamine Intolerance

Diagnosis

- No gold standard test
- Based on clinical history + response to low-histamine diet
- Other investigations: DAO testing, plasma histamine, food/symptom diary





24-hour urinary methylhistamine collection (*note: affected by diet protein/histamine content*)
Based on clinical history + response to low-histamine diet

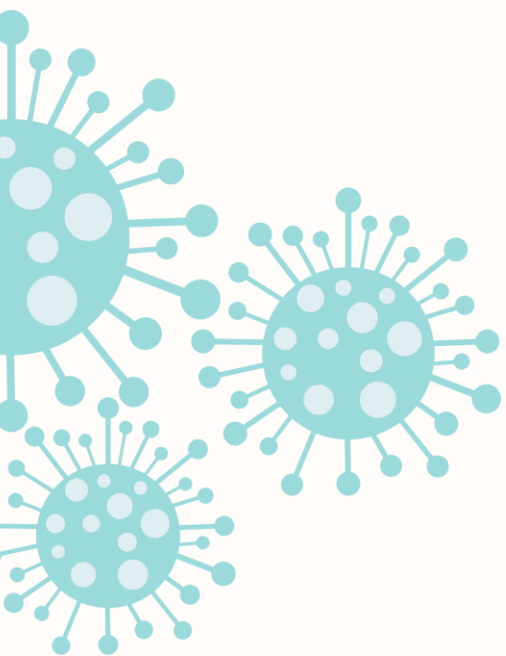
Plasma histamine is not reliable – self degrades in roughly 15 min

- Giera B et al. (2008): no difference between provocation vs control. [Inflamm Res. 2008;57 Suppl 1:S73-4. PMID: 18345482]

Histamine Intolerance

Management

- **Short-term low-histamine diet**
- **Treat underlying gut issues**
- **Review medications**
- **Antihistamines: H1 blockers for flushing and H2 blockers for nausea/vomiting.**
- **Limited evidence for DAO supplementation (suggested dose is 4.2mg two to three times a day)**



Histamine Intolerance

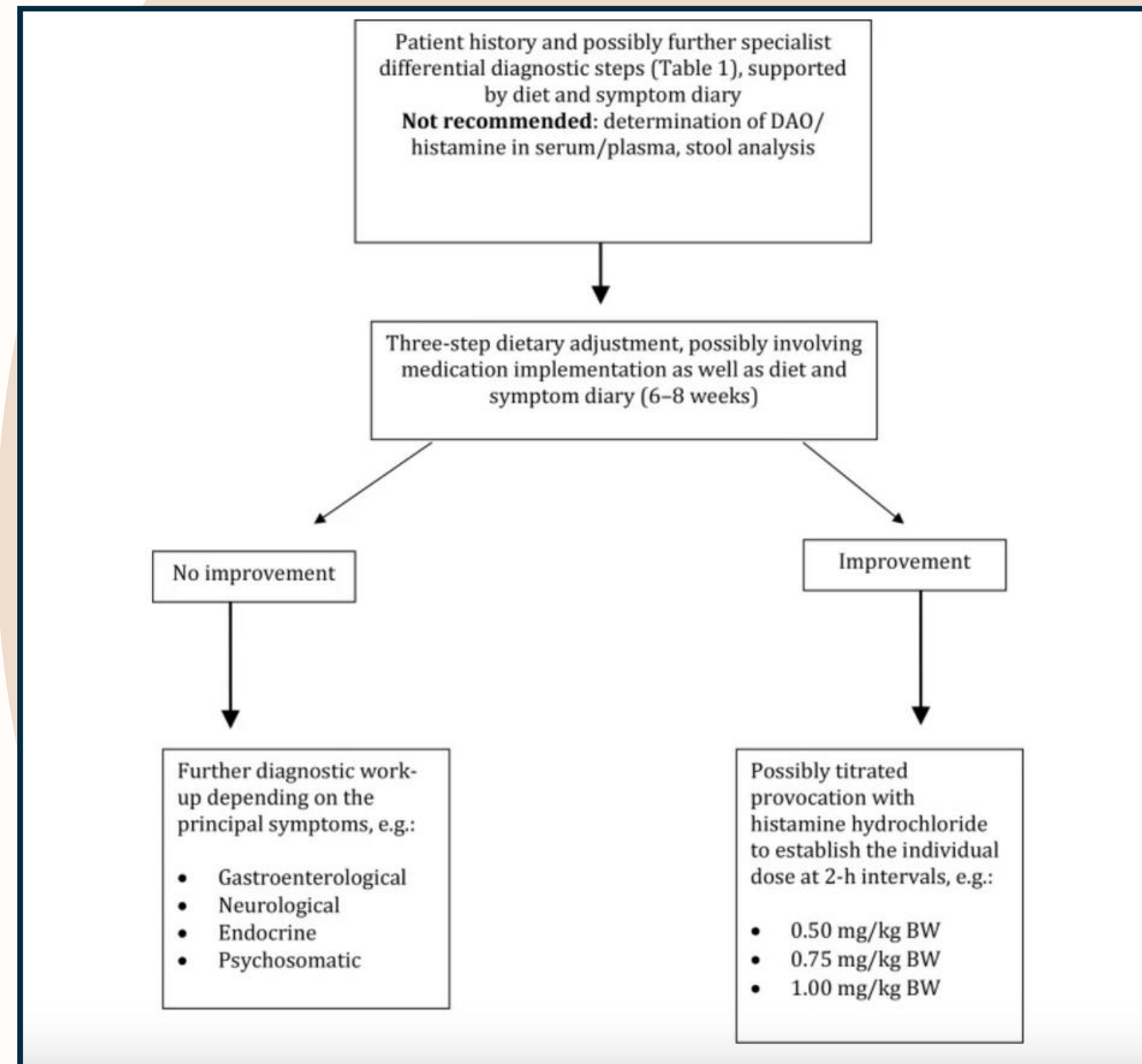
Management

Phase	Aim	Recommendation	Duration
Phase 1: avoidance	To reduce symptoms to the greatest possible extent	– Mixed diet with emphasis on vegetables and reduced biogenic amine intake, in particular histamine intake – Nutrient optimization – Changes in meal composition – Principles of a balanced diet	10– 14 Days
Phase 2: test phase	To expand the choice of food while taking individual risk factors (stress, menstruation, medication use, etc.) into account	– Targeted re-introduction of suspected foods while taking the patient's individual dietary preferences into consideration – Determination of individual histamine tolerance	Up to 6 weeks
Phase 3: long- term diet	Continuous, balanced supply of nutrients High quality of life	– Individual nutritional recommendations guided by the individual histamine tolerance, taking exogenous risk factors into consideration	–

Maintz & Novak, Allergol Select, 2017 (Table 2)

Histamine Intolerance

Management



Maintz & Novak, Allergol Select, 2017 (Fig. 2)

Mast Cell Activation Syndrome (MCAS)

What Is MCAS?



Mast cell activation syndrome (MCAS) is a rare condition that is characterised by recurrent sudden-onset episodes of severe systemic symptoms associated with the release of mast cell mediators. In many cases the recurrent episodes present as anaphylaxis.

What Is MCAS?



Recognised
as a
disorder
around
2007

Mast cells
release
mediators
inappropriately

Often
chronic,
fluctuating,
and hard to
identify

MCAS

– Symptoms Across Systems

Gastrointestinal

diarrhoea,
cramping,
nausea

Cardiovascular

low blood
pressure,
palpitations



MCAS

– Symptoms Across Systems

Neurological



brain fog,
fatigue,
dizziness

Respiratory

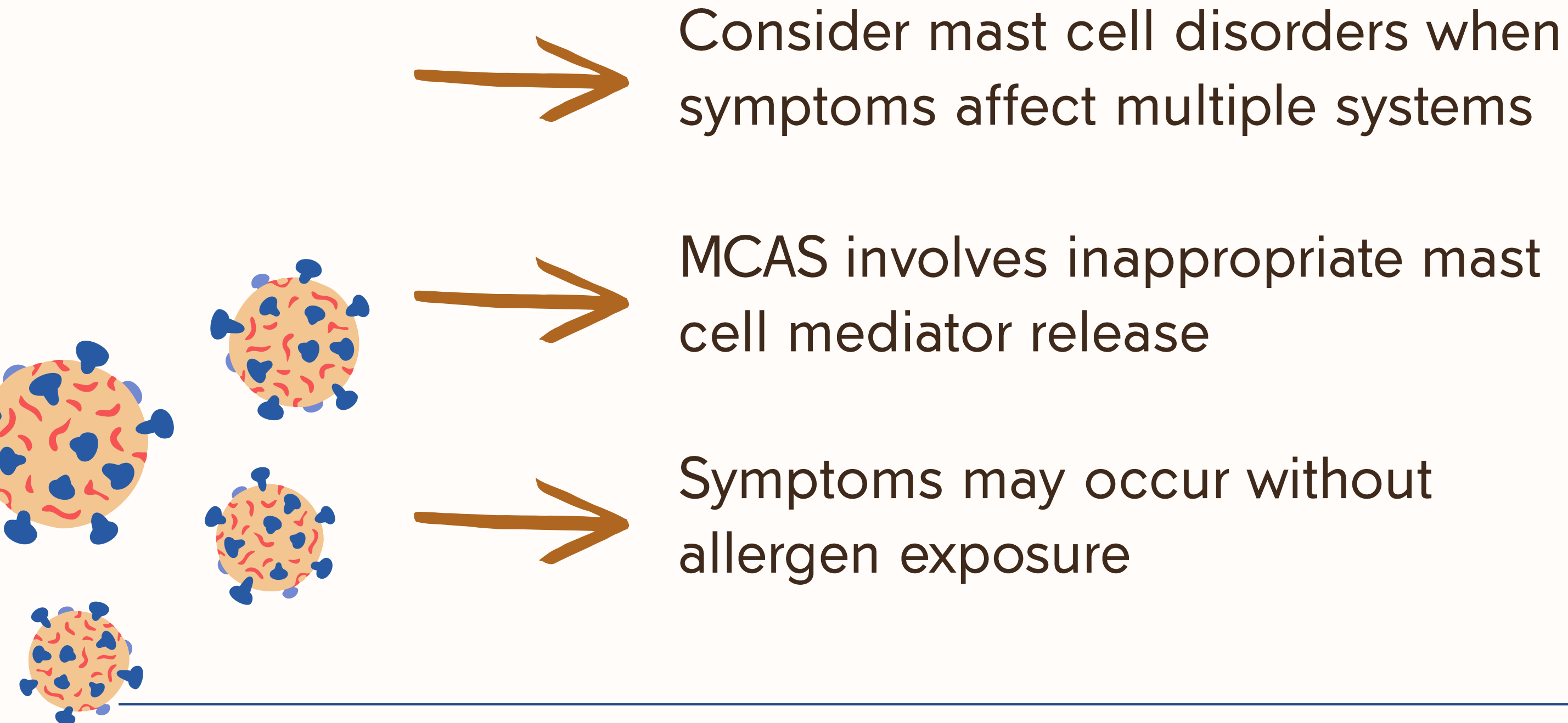
wheezing,
throat
tightness

Skin



flushing,
hives,
itching

Diagnosing MCAS



Diagnosing MCAS

To make a diagnosis of Mast Cell Activation Syndrome (MCAS), doctors rely on **three main criteria** agreed in international consensus paper...

Diagnosing MCAS

Symptoms in
more than
two systems



Elevated mast cell mediators:

~~Tryptase~~ (old consensus)
Plasma heparin (high molecular
weight)

Prostaglandins: (F2 Alpha is
produced in many cells, whilst
DM and D2 are more specific to
mast cells)

Clinical improvement
with antihistamines or
mast cell stabilisers



Challenges

Symptoms in
more than
two systems



Elevated mast cell mediators:

~~Tryptase~~ (old consensus)
Plasma heparin (high molecular
weight) **Prostaglandins:** (F2
Alpha is produced in many cells
whilst DM and D2 are more
specific to mast cells)

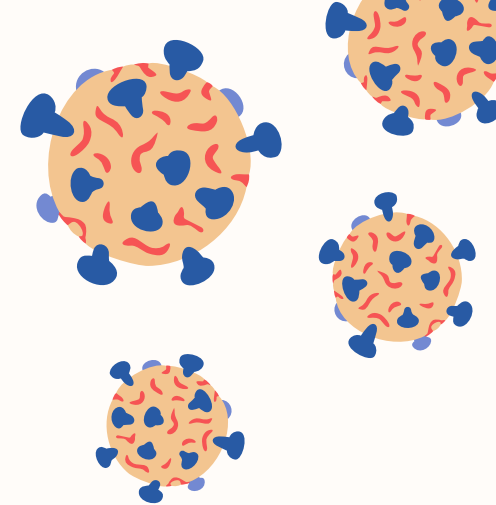
Clinical improvement
with antihistamines or
mast cell stabilisers



Episodic nature:

Symptoms come and go,
so lab tests can be normal
if taken at the wrong time.
Limited testing availability:

Many clinics don't have
access to advanced urinary
mediator testing.
This can delay or complicate
diagnosis



Diagnosis Challenges (MCAS)

Diagnosis is difficult - symptoms overlap with:

Spontaneous urticaria

Spontaneous angioedema

Hereditary alpha tryptasemia

C1 esterase deficiency

Autoimmune disorders, etc

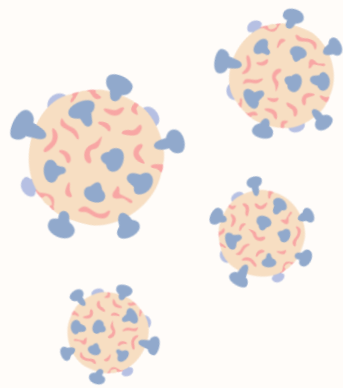
- Lyons JJ et al. Mast Cell Activation Syndrome: Recent Advances. J Allergy Clin Immunol Pract. 2024. [PMC11881543]



**Often
misdiagnosed
as anxiety, IBS,
“unexplained
allergy”**



Management of MCAS



—● *H1 and H2 antihistamines*

—● *Leukotriene inhibitors*

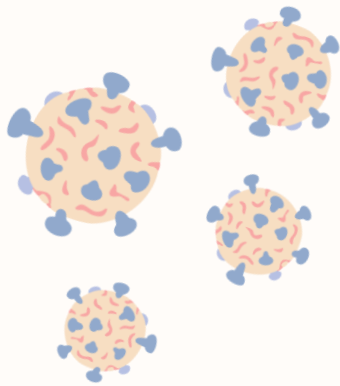
—● *Mast cell stabilisers (e.g. Cromolyn (USA) or Sodium Cromoglicate (UK), Ketotifen).*

—● *Avoid known triggers (heat, infections, stress, smells, histamine foods)*

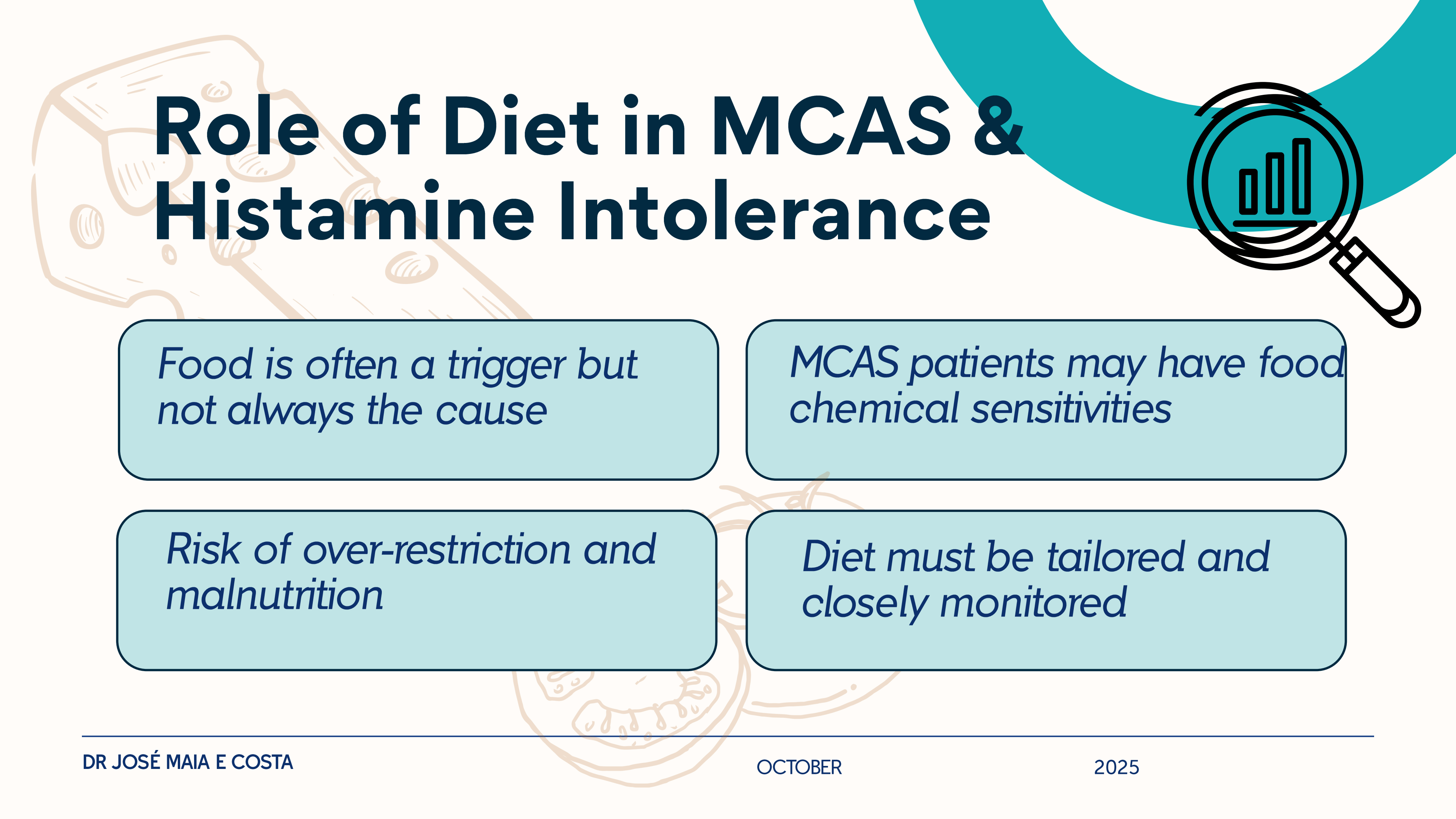
Treatment - MCAS

Emerging Therapies

- **Low-dose naltrexone (LDN):** possible effect via opioid receptors on mast cells (BMJ Case Rep 2018)
- **Omalizumab (anti-IgE):** supportive evidence in MCAS (JACI 2025, PMID: 39741373)



Role of Diet in MCAS & Histamine Intolerance



Food is often a trigger but not always the cause

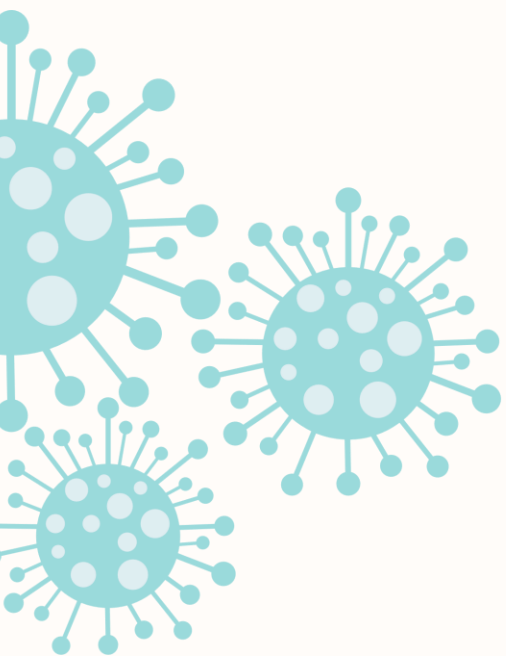
MCAS patients may have food chemical sensitivities

Risk of over-restriction and malnutrition

Diet must be tailored and closely monitored

The Dietitian's Role

- **Educate on low-histamine and anti-inflammatory approaches**
- **Guide reintroduction phase**
- **Prevent nutritional deficiencies**
- **Track symptom patterns**
- **Collaborate with allergy/immunology teams**



Summary:

- ➔ Histamine intolerance and MCAS are under-recognised and complex
- ➔ Require careful diagnosis and personalised treatment
- ➔ Dietitians are key to supporting quality of life
- ➔ A multidisciplinary approach makes a big difference

Questions



The Childrens Allergy

Dr José Maia e Costa

