Mastcelleaktiveringssyndrom
Noe for hudlegen å tenke på?

Thomas Schopf

Spesialist i hudsykdommer

Overlege RAAO

Universitetssykehuset Nord-Norge

Mastcelleaktiveringssyndrom (MCAS)

- Bakgrunn og patogenese
- Klinikk
- Diagnostiske kriterier og utredning
- Differensialdiagnoser
- Behandling
- Kontroverser

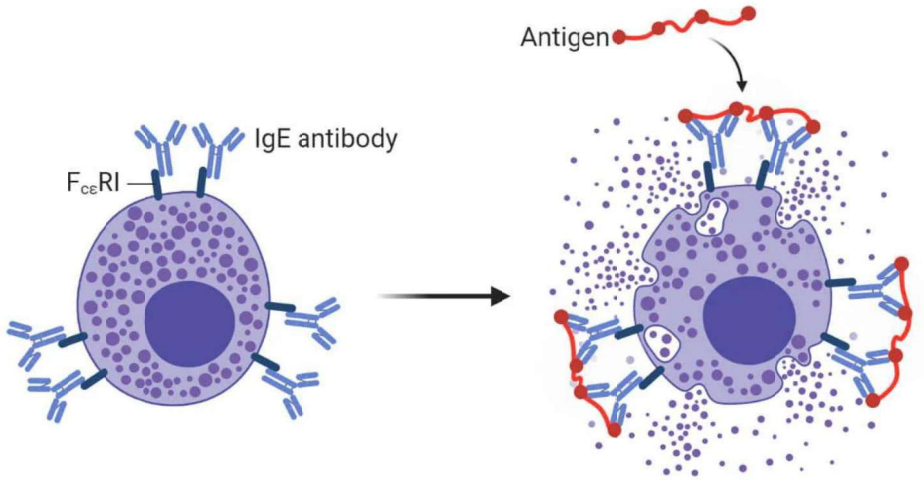
Mastcelleaktiveringssyndrom (MCAS)

- Lite kjent sykdom
- Ikke enighet om diagnostiske kriterier
- Mange pasienter med MCAS kommer før eller siden til RAAO pga plager med overfølsomhet og allergier. « Jeg reagerer på alt! »

Mastcelleaktiveringssyndrom (MCAS) Inndeling

- Primær MCAS
  - Mastocytose
- Sekundær MCAS
  - IgE-mediert allergi
  - Hypereosinofilt syndrom
  - Autoimmune sykdommer
- Idiopatisk MCAS

IgE Cross-linking Induces Mast Cell Activation and Degranulation



Resting mast cell

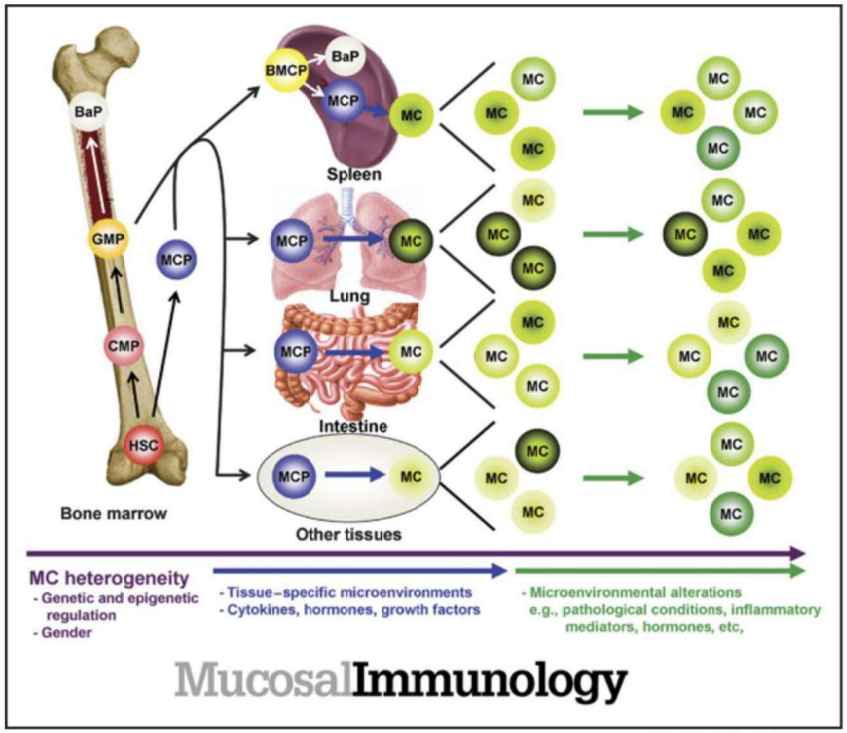
Resting mast cell granules contain histamine and other inflammatory mediators

Activated mast cell

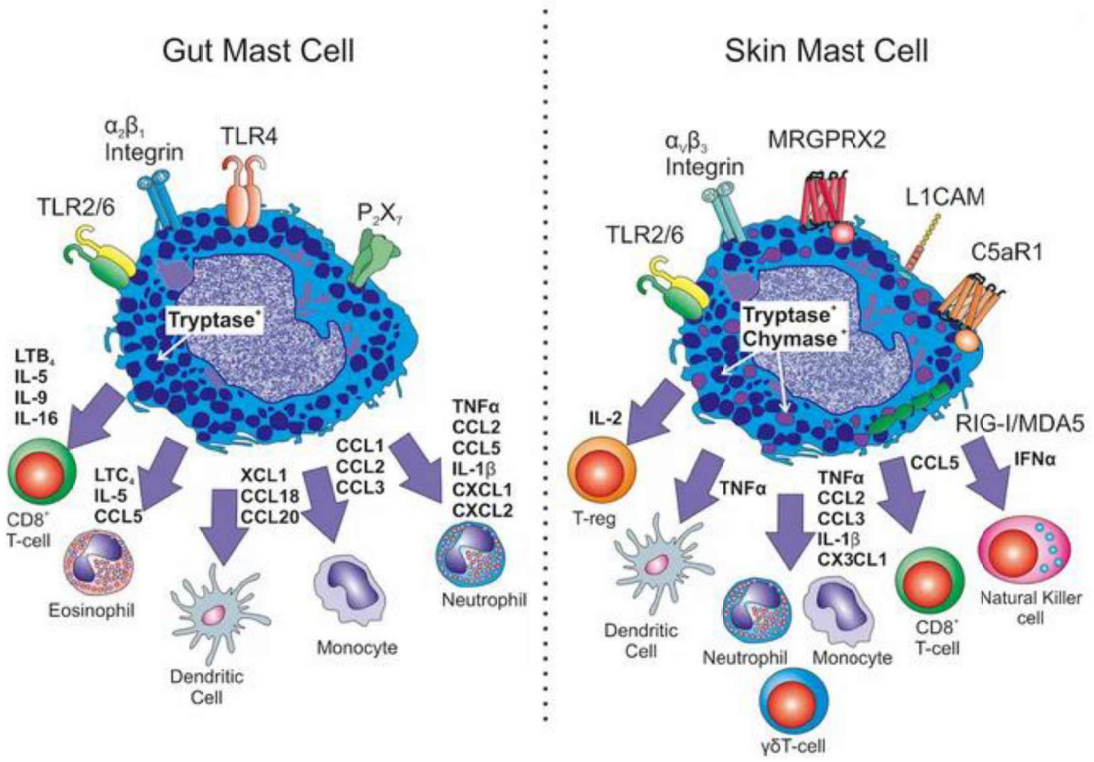
Multivalent antigen cross-links bind igE antibodies, causing degranulation

MucosalImmunology

Figure 1



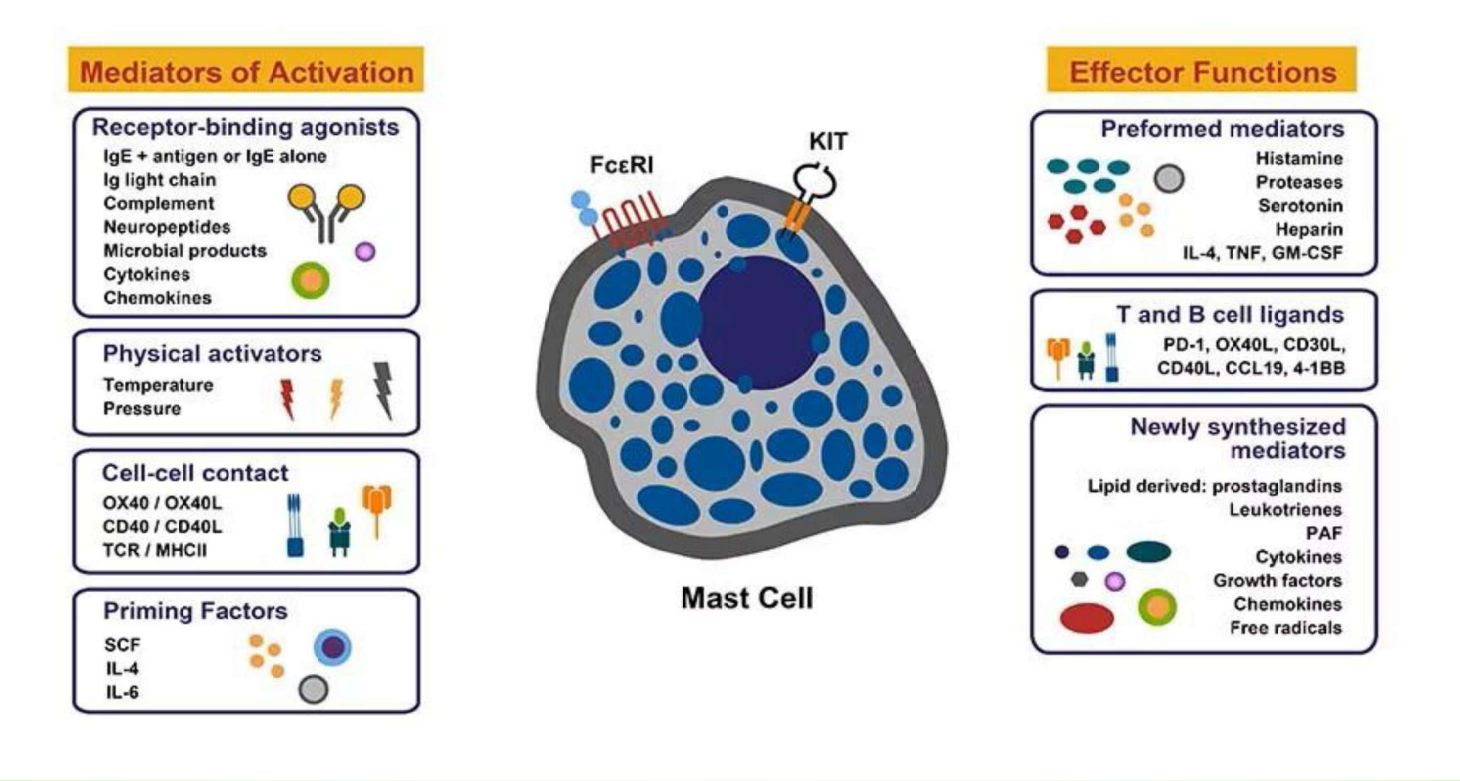
Mucosal Immunology (2010) **3,** 111-128;
10.1038/mi.2009.136



MINI REVIEW
29 July 2022

Mast cell tissue heterogeneity and specificity of immune cell recruitment

Peter W. West and Silvia Bulfone-Paus



Thermo Fisher Scientific

Mastcelleaktiveringssyndrom (MCAS) Bakgrunn

- Typisk pasient på RAAO etter Covid pandemien:
  - Forverring ifm Covid infeksjon og vaksine (?)
  - Har hatt symptomer i 10-20 år
  - Utredet på mange avdelinger (kirurgisk, medisinsk, nevrologisk), ofte uten diagnose

Mastcelleaktiveringssyndrom (MCAS) Bakgrunn

- Debut ofte i ung alder - evt i barndommen ?
- Uklare symptomer og ingen diagnose
- « Ble ikke trodd » og « Det er psykisk! »

Mastcelleaktiveringssyndrom (MCAS) Klinikk

- Anfallsvise symptomer
- Raskt innsettende, kan vare i minutter – timer
- Trigges av « allergener » – stress og fysiske stimuli (inkl. smerter)
- « Jeg reagerer på alt! »

Mastcelleaktiveringssyndrom (MCAS) Klinikk

- Huden:
  - Kløe. Ofte generelt i hele huden, men også i øyne og svelg.
  - Flushing, varmefølelse
  - Nummenhet
  - Hevelser

Mastcelleaktiveringssyndrom (MCAS) Klinikk

- Hjertebank, svimmelhet
- Tungpustenhet
- Abdominale smerter, brekninger, diare
- Fatigue

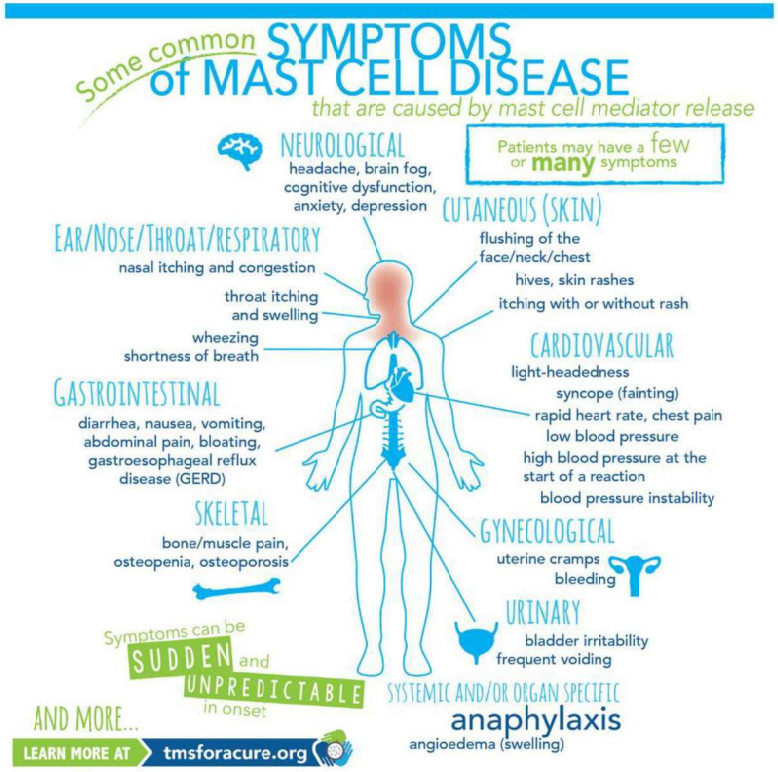
Mastcelleaktiveringssyndrom (MCAS) Klinikk

- Hudfunn:
  - **Urticaria**
  - **Angioødem**
  - Erytem
  - Eksem
  - Purpuraliknende lesjoner

Mastcelleaktiveringssyndrom (MCAS) Klinikk

- Rhinokonjunktivitt
- Høy puls, BT-fall
- Astma
- Anafylaksi

These are common symptoms I often hear about in addition to my own. Yes, there is a lot of overlap with POTS symptoms. Symptoms vary by person. For some the condition can be mild, while for others completely debilitating. For a very thorough listing of common symptoms see journal article Characterization of Mast Cell Activation Syndrome.



Mastcelleaktiveringssyndrom (MCAS) Klinikk

- Triggere:
  - Matvarer som inneholder eller fører til frigjørelse av histamin
  - Temperatur
  - Vann
  - Vibrasjon
  - Sol
  - Legemidler

Mastcelleaktiveringssyndrom (MCAS) Klinikk

- I kronisk fase:
  - Anfallene er ikke lenger så tydelig.
  - For pasienten er hudsymptomene mindre plagsomt.
  - Fatigue er fremtredende. Mange har en ME/CFS - diagnose

Mastcelleaktiveringssyndrom (MCAS) Klinikk

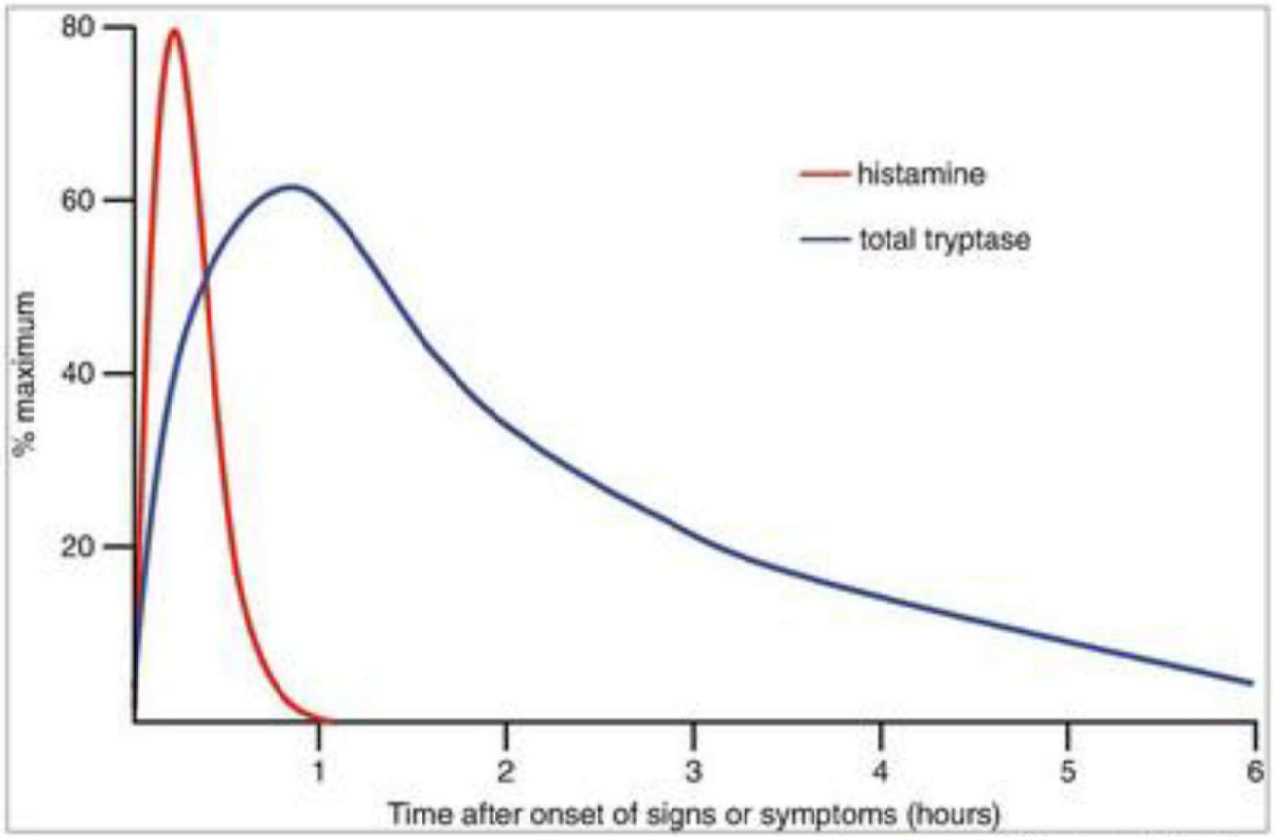
- I kronisk fase (forts.):
  - Kognitive vansker, «hjernetåke»
  - Smerter (hodepine, brystsmerter, abdomen, muskler)
  - Mange pasienter med redusert arbeidsevne / uførhet

Mastcelleaktiveringssyndrom (MCAS) Utredning

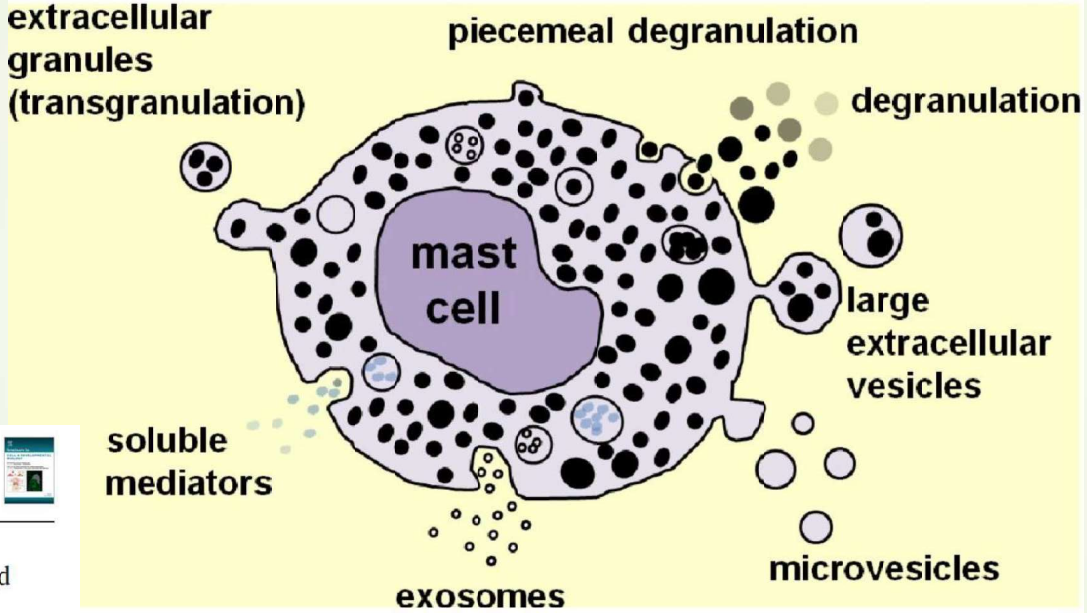
- Anamnese
- Klinisk us., evt se på hudbilder tatt av pasienten
- Prøver:
  - IgE / prikktest
  - Tryptase
  - C1-esterasehemmer / C4
  - Histamin (ikke rutine)
  - Leukotriener (ikke rutine)

Mastcelleaktiveringssyndrom (MCAS) Diagnostikk

- Tryptase:
  - I en del litteratur legges det vekt på forhøyet tryptase under anfall
  - Ikke alltid så lett å måle på optimalt tidspunkt
  - Validert for kraftige utbrudd og anafylaksi



Figur: Lyons & Schwartz (2019)



Seminars in Cell & Developmental Biology
Volume 67, July 2017, Pages 65-73

Review

Mast cell secretome: Soluble and vesicular components

Krisztina V. Vukman, András Försönits, Ádám Oszvald, Eszter Á. Tóth, Edit I. Buzás

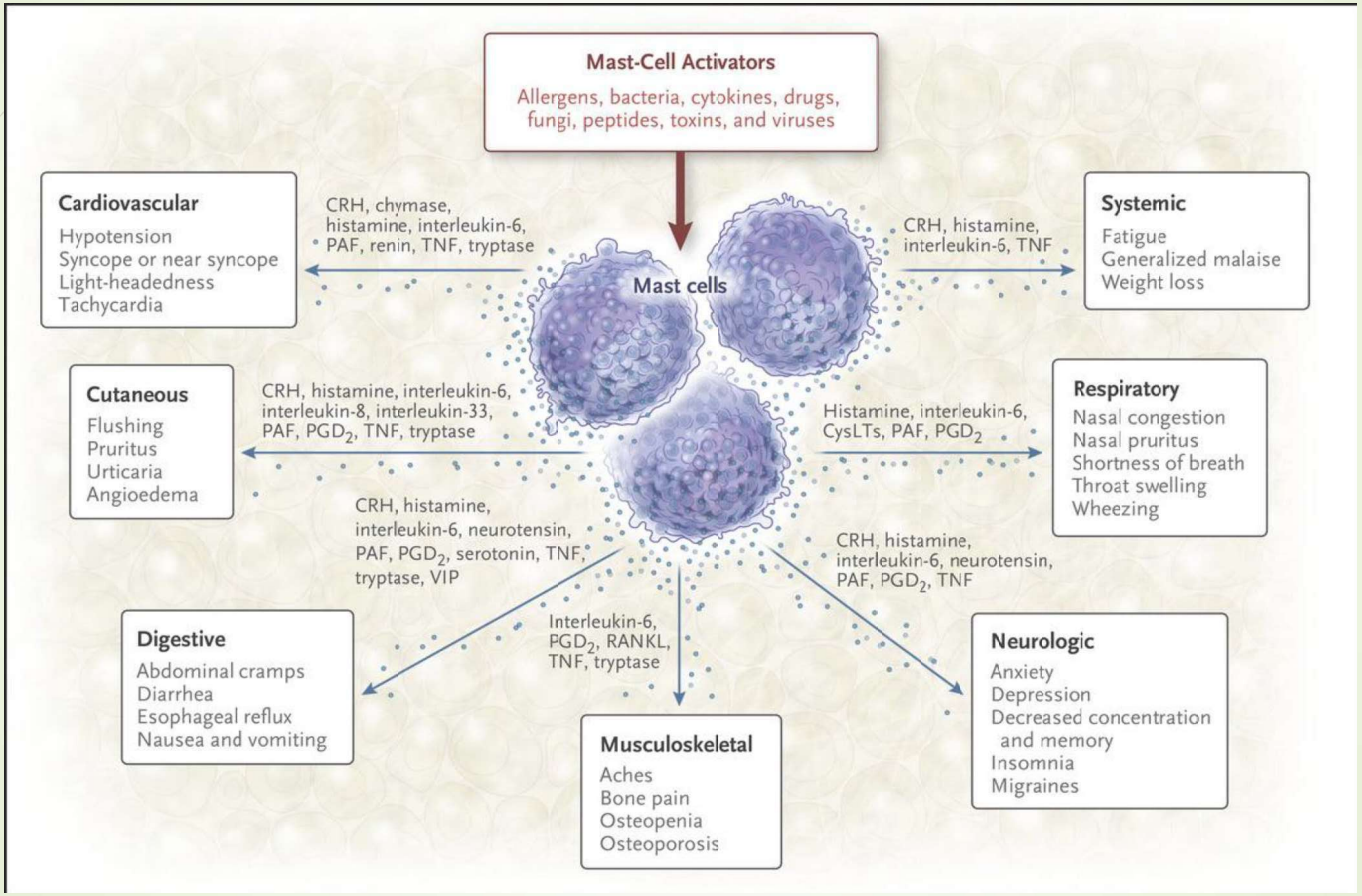
Semmelweis University Department of Genetics, Cell- and Immunobiology, H-1089 Budapest, Hungary

Received 3 October 2016, Revised 17 January 2017, Accepted 7 February 2017, Available online 9 February 2017, Version of Record 22 June 2017.

What do these dates mean?

Check for updates

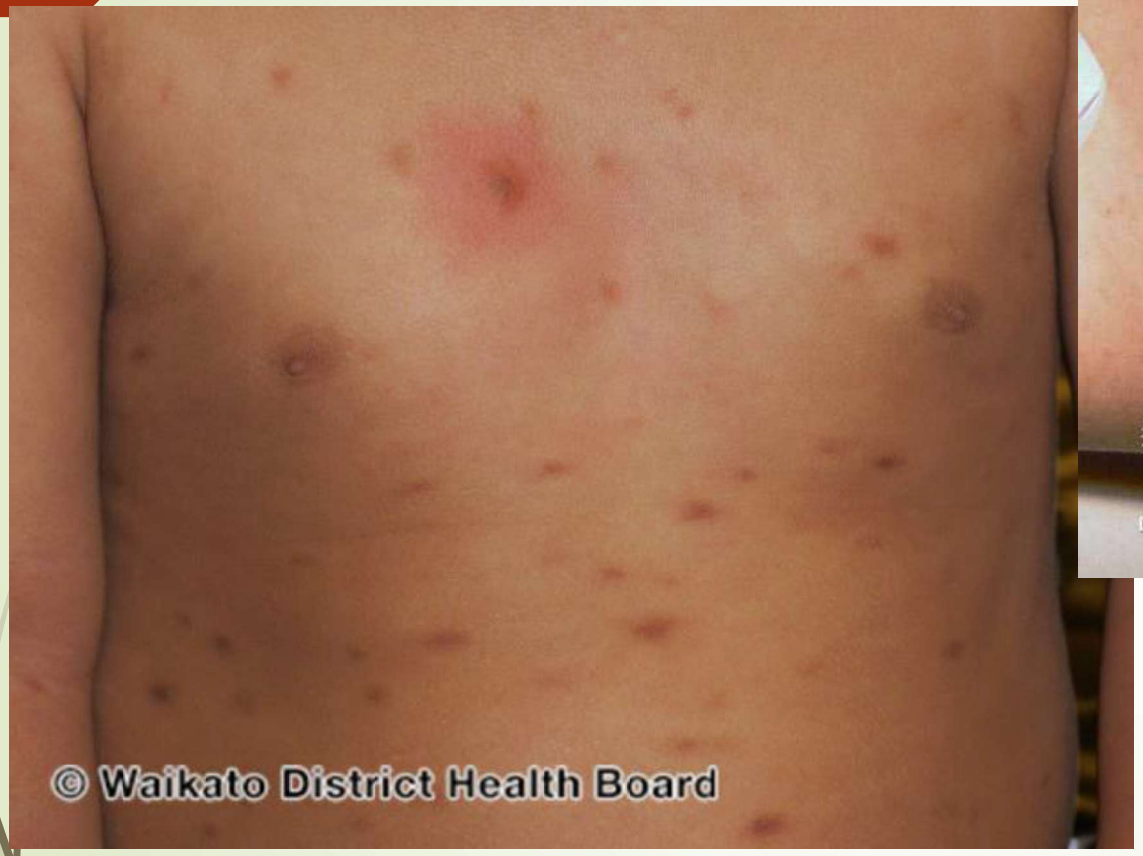
Clinically Relevant Mediators Released from Mast Cells and Putative Effects.

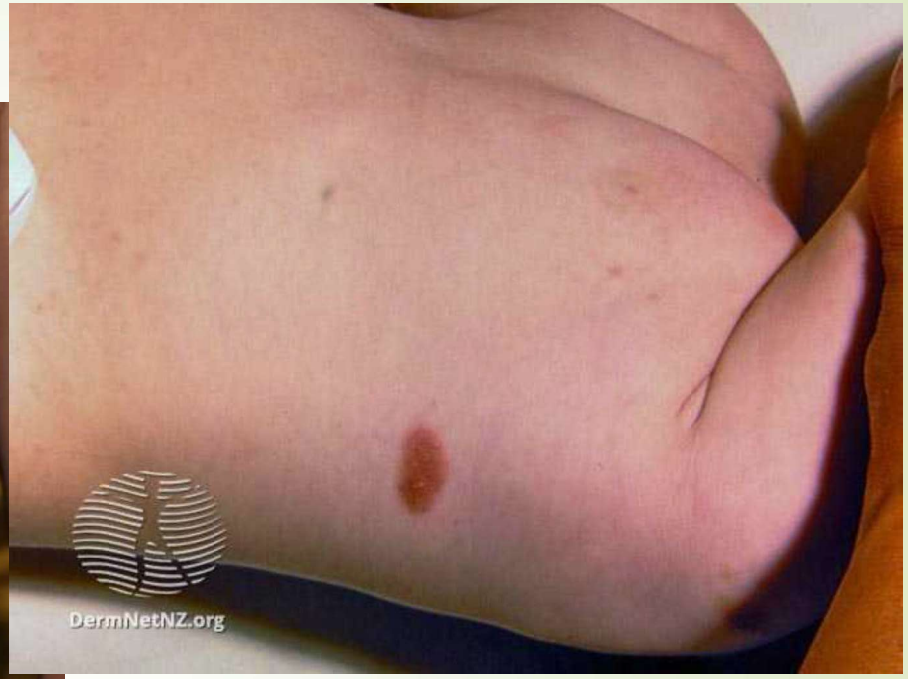


Theoharides TC et al. N Engl J Med 2015;373:163-172.

Mastcelleaktiveringssyndrom (MCAS) Differensialdiagnoser

- Vurdere andre årsaker:
  - Straksallergi (spesifikk IgE + prikktest)
  - Mastocytose (blodprøve KIT D816V + benmargsbiopsi)
  - Neuroendokrin tumor, feokromocytom, karsinoid tumor (Normetanefrin, Metanefrin, Kromogranin A)
  - Hypereosinofilt syndrom (eosinofile celler)





- Kutan mastocytose

Mastcelleaktiveringssyndrom (MCAS) Mastocytose

- Pga mutasjon produseres for mange mastceller
- Typiske hudfunn
- Malignt forløp mulig. Hos barn som regel god prognose.
- Benmargsbiopsi

Mastcelleaktiveringssyndrom (MCAS) Behandling

- Kontrollere triggere
- Behandle andre sykdommer
- Medikamenter

Mastcelleaktiveringssyndrom (MCAS) Behandling

- Medikamentell basisbehandling (faste medisiner):
  - Antihistaminer
  - Omalizumab (Xolair)

Mastcelleaktiveringssyndrom (MCAS) Behandling

- Antihistaminer
- Prinsipielt kan alle typer forsøkes
- Start med et preparat som gradvis økes til fire-dobbel dose ila noen uker
- Flere preparater kan brukes samtidig

Mastcelleaktiveringssyndrom (MCAS) Behandling

- Antihistaminer
  - Prøve minst 2-3 typer i høy dose
  - Dosering 2-4 ganger daglig
  - Individuelle forskjeller

Mastcelleaktiveringssyndrom (MCAS) Behandling

- Eksempel
  - Gradvis opptrapping til Cetirizin 20 mg morgen og kveld
  - Etter 3-4 uker legges Ebastin til på dårlige dager: 10-20 mg ved behov.
  - Ebastin kan også brukes fast (i tillegg til Cetirizin)

Mastcelleaktiveringssyndrom (MCAS) Behandling

Naunyn-Schmiedeberg's Arch Pharmacol (2016) 389:671–694
DOI 10.1007/s00210-016-1247-1

REVIEW

Pharmacological treatment options for *mast cell activation disease*

Gerhard J. Molderings[1] · Britta Haenisch[2] · Stefan Brettner[3] · Jürgen Homann[4] · Markus Menzen[4] · Franz Ludwig Dumoulin[4] · Jens Panse[5] · Joseph Butterfield[6] · Lawrence B. Afrin[7]

> Allergy Asthma Proc. 2025 Jan 1;46(1):11-18. doi: 10.2500/aap.2025.46.240

Systematic review of omalizumab for refractory clonal and non-clonal mast cell activation syndrome

Meghan V Matheny [1], Timothy Craig [1], Taha Al-Shaikhly [1]

Affiliations – collapse

Affiliation

1 From the Section of Allergy, Asthma and Immunology, Medicine and Pediatrics, Pennsylvania State University School of Medicine, Hershey, Pennsylvania and.

PMID: 39741373 DOI: 10.2500/aap.2025.46.240076

Mastcelleaktiveringssyndrom (MCAS) Behandling

- Omalizumab – på indikasjon «urticaria», dosering off-label
  - Initialt 300 mg hver 4. uke
  - Etter 2-3 runder vurderes hyppigere applikasjon eller høyere dose
  - De fleste pasienter trenger injeksjon hver 2. eller 3. uke
  - Total dose per mnd er ofte rundt 600 – 900 mg

Mastcelleaktiveringssyndrom (MCAS) Behandling

- Andre medikamenter:
  - Ketotifen
  - Montelukast
  - Na-Kromoglykat (Allergoval)
  - Benzodiazepiner (ikke-sederende dose)

Mastcelleaktiveringssyndrom (MCAS) Behandling

- Behandling av utbrudd
  - Adrenalin
  - Antihistamin: Ekstra dose eller eget «akutt preparat»
  - NSAID
  - Prednisolon
  - Ikatibant

Mastcelleaktiveringssyndrom (MCAS) Behandling

- Unngå triggere
- Obs legemidler:
  - Hyppig overfølsomhet
  - Ofte involvert: Opioider, NSAID, fargestoffer

Mastcelleaktiveringssyndrom (MCAS) Behandling

- Evaluering av medikamentell behandling
  - Effekt kommer ila få uker
  - Dersom ingen/svak effekt byttes preparat
  - Pasienten merker ofte at virkningen av Omalizumab avtar – vurder doseøkning
  - Når man har funnet rett medisinering, kan man forvente ytterligere bedring over tid (flere mnd - 1 år).

Mastcelleaktiveringssyndrom (MCAS) Behandling

- Evaluering generelt
  - Etter hvert som pasientene blir bedre, utsetter de seg for flere triggere
  - Vanlig med svingende forløp

Mastcelleaktiveringssyndrom (MCAS) Uenighet om kriterier

- Stor uenighet blant internasjonale eksperter (og allergologer i Norge)
- To skoler:
  - Valent, Akin, Gülen: Consensus - criteria
  - Afrin, Molderings: Consensus 2 - criteria

Volume 157, Issue 3
February 2012

ARTICLE CONTENTS

REVIEW ARTICLES | OCTOBER 27 2011

Definitions, Criteria and Global Classification of Mast Cell Disorders with Special Reference to Mast Cell Activation Syndromes: A Consensus Proposal Free

Subject Area: Immunology and Allergy

Peter Valent; Cem Akin; Michel Arock; Knut Brockow; Joseph H. Butterfield; Melody C. Carter; Mariana Castells; Luis Escribano; Karin Hartmann; Philip Lieberman; Boguslaw Nedoszytko; Alberto Orfao; Lawrence B. Schwartz; Karl Sotlar; Wolfgang R. Sperr; Massimo Triggiani; Rudolf Valenta; Hans-Peter Horny; Dean D. Metcalfe

Int Arch Allergy Immunol (2012) 157 (3): 215–225.
https://doi.org/10.1159/000328760 Article history

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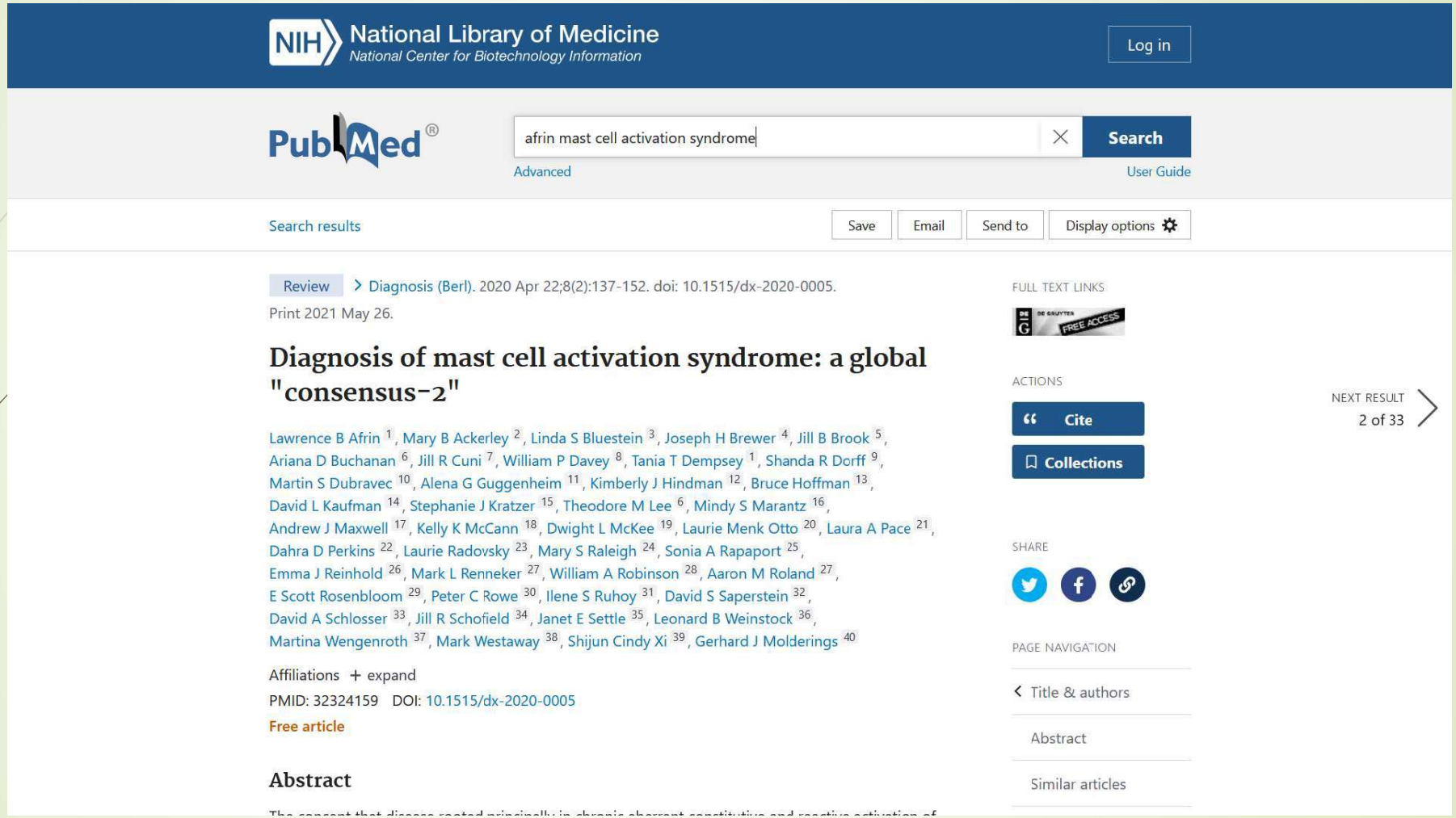
Abstract

Activation of tissue mast cells (MCs) and their abnormal growth and accumulation in various organs are typically found in primary MC disorders also referred to as mastocytosis. However, increasing numbers of patients are now being informed that their clinical findings are due to MC activation (MCA) that is neither associated with mastocytosis nor with a defined allergic or inflammatory reaction. In other patients with MCA, MCs appear to be clonal cells, but criteria for diagnosing mastocytosis are not met. A working conference was organized in 2010 with the aim to define criteria for diagnosing MCA and related disorders, and to propose a global unifying classification of all MC disorders and pathologic MC reactions. This classification includes three types of 'MCA syndromes' (MCASs), namely primary MCAS, secondary MCAS and idiopathic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Review
Diagnosis (Berl). 2020 Apr 22;8(2):137-152. doi: 10.1515/dx-2020-0005.
Print 2021 May 26.
Diagnosis of mast cell activation syndrome: a global "consensus-2"
Lawrence B Afrin [1], Mary B Ackerley [2], Linda S Bluestein [3], Joseph H Brewer [4], Jill B Brook [5], Ariana D Buchanan [6], Jill R Cuni [7], William P Davey [8], Tania T Dempsey [1], Shanda R Dorff [9], Martin S Dubravec [10], Alena G Guggenheim [11], Kimberly J Hindman [12], Bruce Hoffman [13], David L Kaufman [14], Stephanie J Kratzer [15], Theodore M Lee [6], Mindy S Marantz [16], Andrew J Maxwell [17], Kelly K McCann [18], Dwight L McKee [19], Laurie Menk Otto [20], Laura A Pace [21], Dahra D Perkins [22], Laurie Radovsky [23], Mary S Raleigh [24], Sonia A Rapaport [25], Emma J Reinhold [26], Mark L Renneker [27], William A Robinson [28], Aaron M Roland [27], E Scott Rosenbloom [29], Peter C Rowe [30], Ilene S Ruhoy [31], David S Saperstein [32], David A Schlosser [33], Jill R Schofield [34], Janet E Settle [35], Leonard B Weinstock [36], Martina Wengenroth [37], Mark Westaway [38], Shijun Cindy Xi [39], Gerhard J Molderings [40]
Affiliations + expand
PMID: 32324159 DOI: 10.1515/dx-2020-0005
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Mastcelleaktiveringssyndrom (MCAS) Uenighet om kriterier

- Uenigheten går på diagnostiske kriterier og på type symptomer
- Consensus 1 - gruppen:
  - Avgjørende vekt på tryptase
  - MCAS gir anafylaksiliknende bilde
  - Man er redd for overdiagnostikk

Mastcelleaktiveringssyndrom (MCAS) Uenighet om kriterier

- Consensus 2 - gruppen:
  - Flere mediatorer kan måles
  - MCAS kan ha ulike alvorlighetsgrader
  - MCAS frembyr et bredt klinisk bilde, inkludert mer uspesifikke symptomer

J Allergy Clin Immunol Pract. 2022 Aug;10(8):1941-1950. doi: 10.1016/j.jaip.2022.05.007. Epub 2022 May 25.

Global Classification of Mast Cell Activation Disorders: An ICD-10-CM-Adjusted Proposal of the ECNM-AIM Consortium

Peter Valent [1], Karin Hartmann [2], Patrizia Bonadonna [3], Theo Gülen [4], Knut Brockow [5], Ivan Alvarez-Twose [6], Olivier Hermine [7], Marek Niedoszytko [8], Melody C Carter [9], Gregor Hoermann [10], Joseph H Butterfield [11], Jonathan J Lyons [12], Wolfgang R Sperr [13], Georg Greiner [14], Karl Sotlar [15], Hanneke C Kluin-Nelemans [16], Juliana Schwaab [17], Magdalena Lange [18], Tracy I George [19], Frank Siebenhaar [20], Sigurd Broesby-Olsen [21], Mohamad Jawhar [17], Boguslaw Nedoszytko [22], Mariana Castells [23], Alberto Orfao [24], Jason Gotlib [25], Andreas Reiter [17], Hans-Peter Horny [26], Massimo Triggiani [27], Michel Arock [28], Dean D Metcalfe [9], Cem Akin [29]

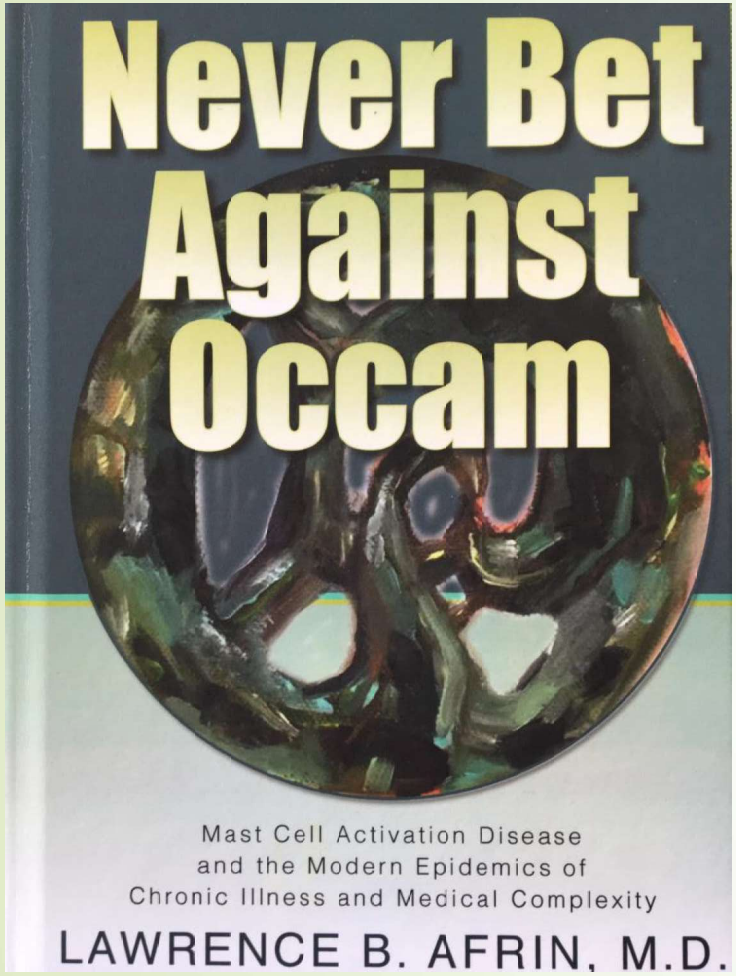
Affiliations + expand

PMID: 35623575 DOI: 10.1016/j.jaip.2022.05.007

Free article

Abstract

Mast cell activation (MCA) is common and occurs in a number of pathologic conditions, including IgE-dependent and independent allergic reactions, atopic disorders, autoimmune processes, and mastocytosis. In a subset of patients, no underlying disease and no known trigger of MCA are found. When the symptoms are severe, systemic, and recurrent, and accompanied by a diagnostic increase in the serum tryptase level or other mast cell mediators, an MCA syndrome (MCAS) may be diagnosed. In these patients, the symptoms typically respond to drugs suppressing MCA, mediator production in mast cells, or mediator effects. In each case, diagnostic consensus criteria must be fulfilled to diagnose MCAS. In other patients, MCA may be local, less severe, or less acute, or may be suspected but not confirmed, so that the diagnostic criteria of MCAS are not fulfilled. In these patients, it may be difficult to prove MCA, for example, by measuring multiple mast cell mediators or basophil activation, the latter as a surrogate of IgE-dependent hypersensitivity. However, validated diagnostic criteria for implicating suspected MCA behind such conditions are lacking, even if some of these conditions have



- Takk for oppmerksomheten!