

Multiple Drug Hypersensitivity

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Multiple drug hypersensitivity syndrome is defined controversially

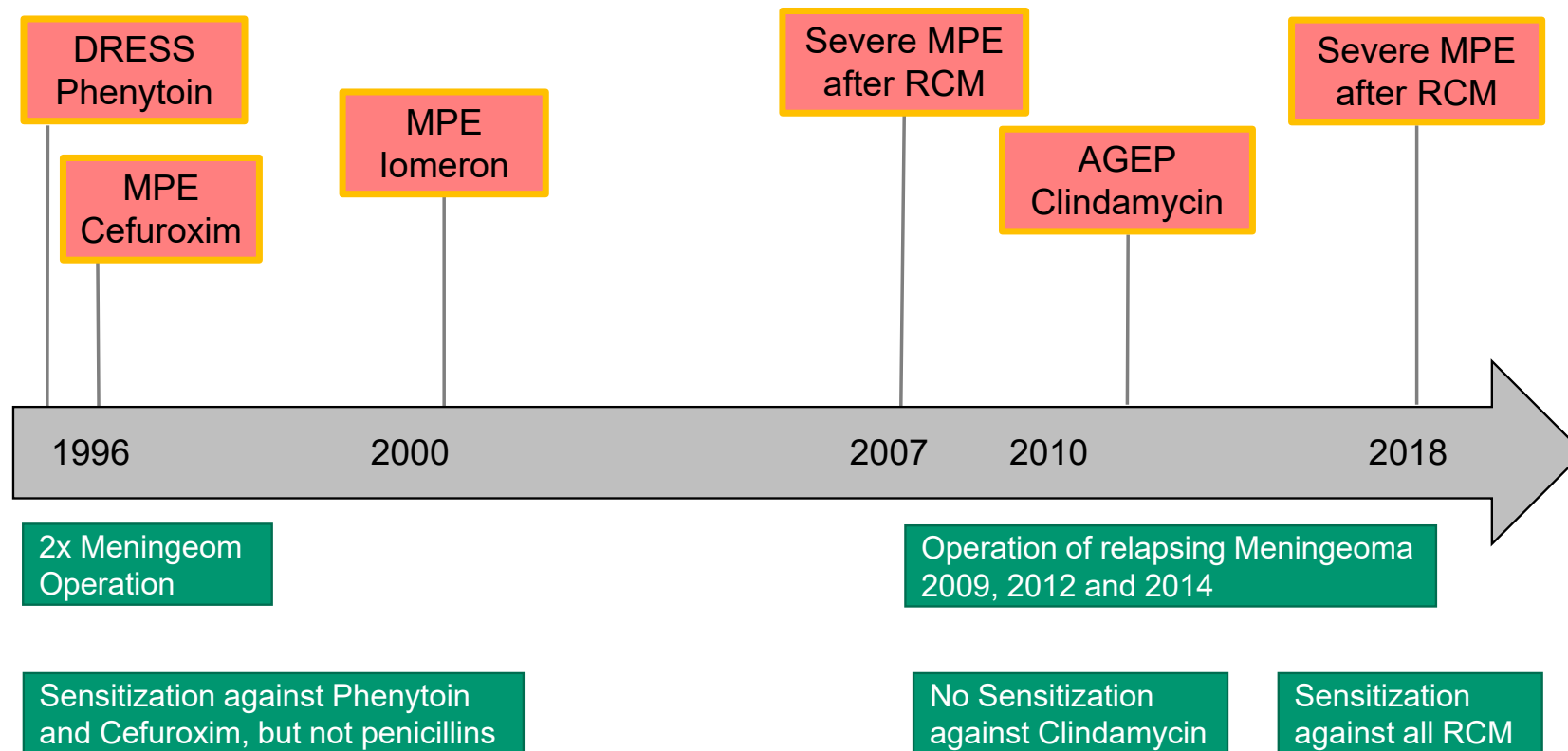
- Many names, diverse meanings
- Do not confuse with multiple intolerance syndrome

Multiple drug hypersensitivity

- Proven drug allergies to two or more chemically different drugs (skin test, in vitro test, \pm drug provocation test)
- No known cross reactivity or similar metabolic/pharmacologic pathway between involved drugs
- No flare-up

Demoly P, et al.. International Consensus on drug allergy. Allergy. 2014 Apr;69(4):420-37.

Case 1: Example of a Multiple drug hypersensitivity syndrome



Approx. 15-30% of all DRESS patients develop an MDH

Developement of MDH

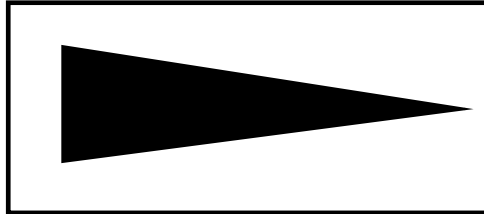
Simultaneous MDH



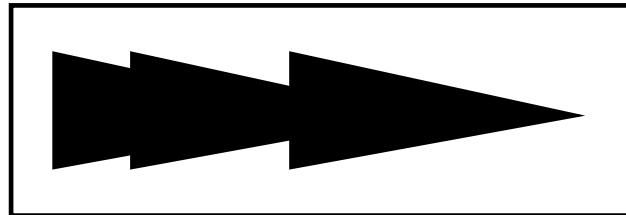
Sequential MDH



Distant form of MDH
(case 1)



same DHR

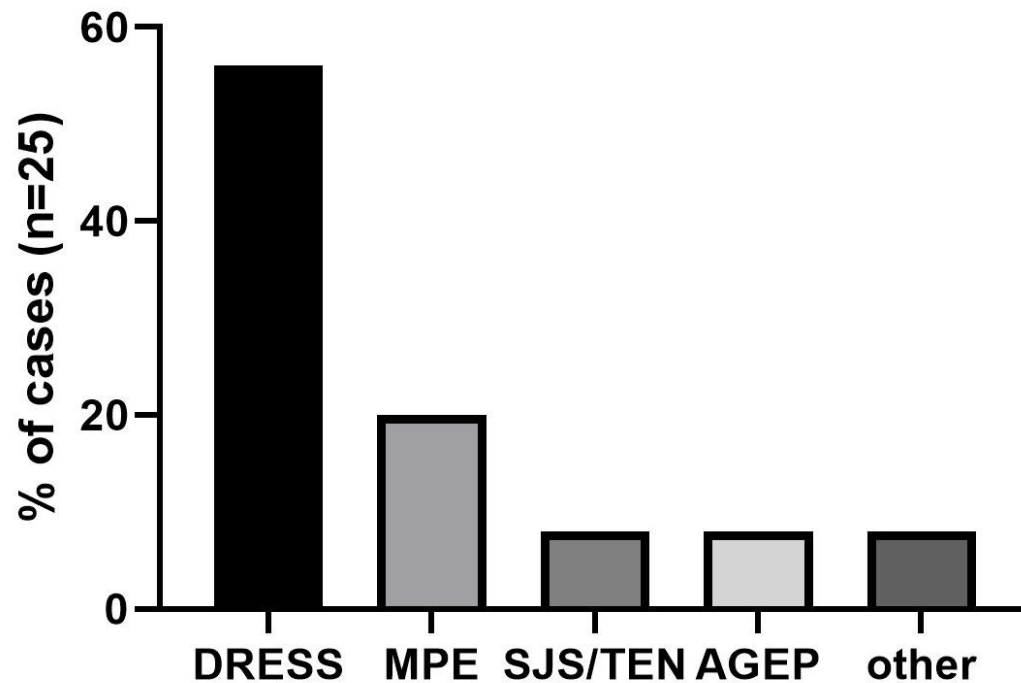


same DHR with relapses
or multiple DHR within the
same event



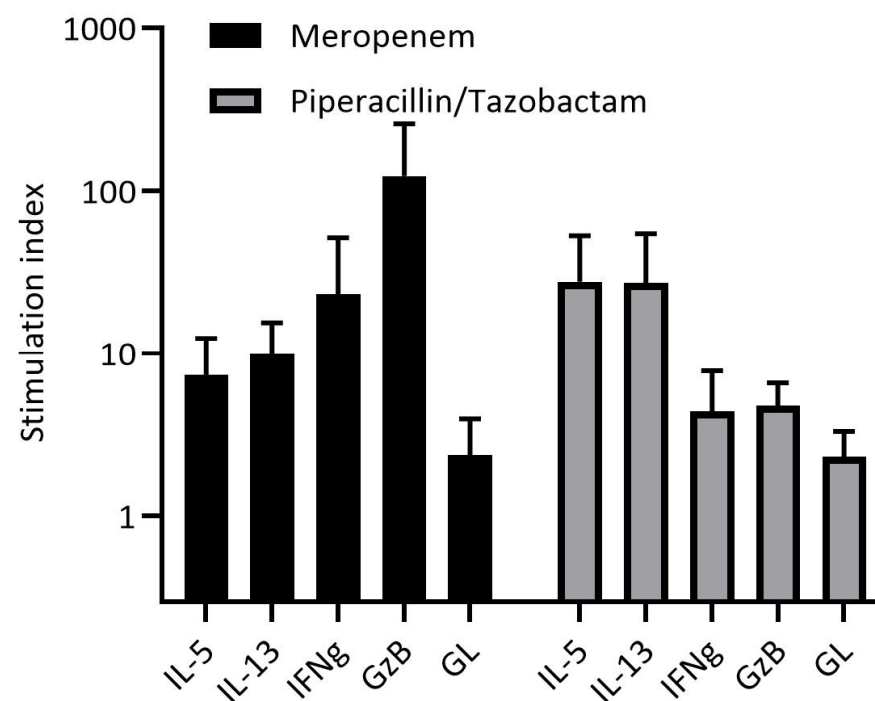
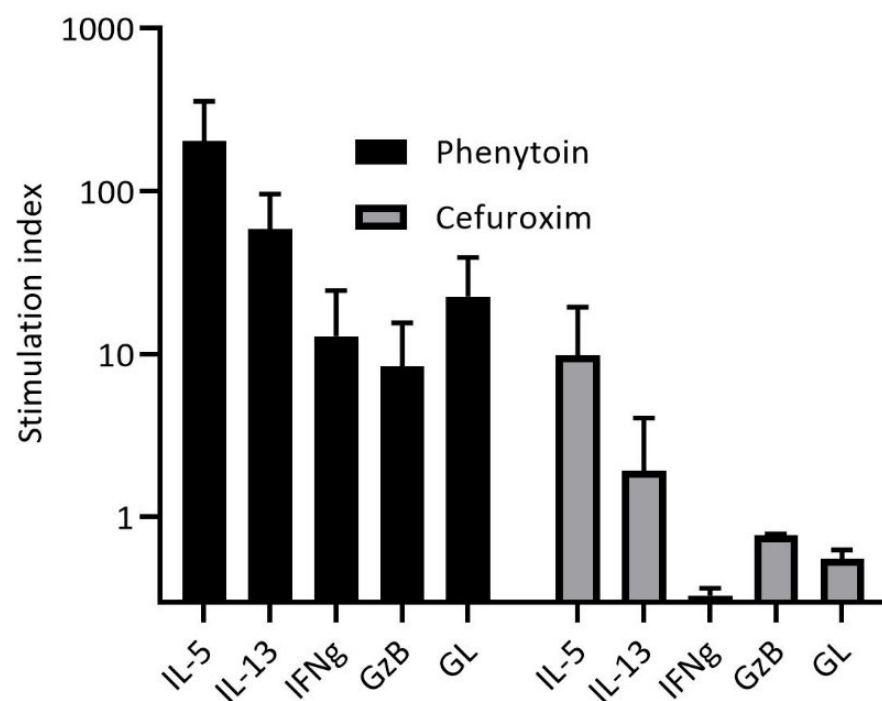
Multiple DHR with months to years in between

The initial reaction of MDH is a severe DHR in most cases

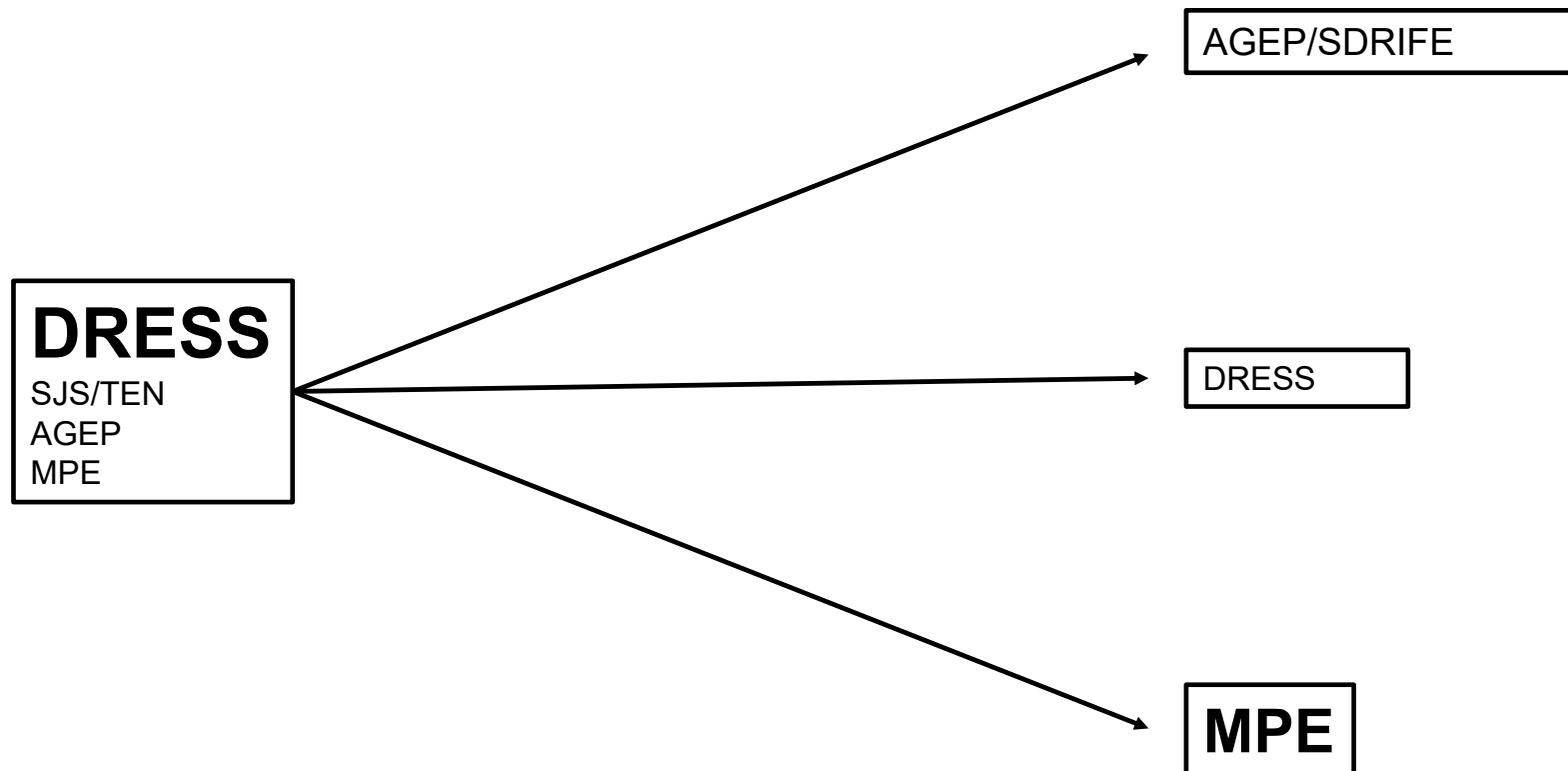


Pichler WJ, et al.. Multiple Drug Hypersensitivity. Int Arch Allergy Immunol. 2017;172(3):129-138.

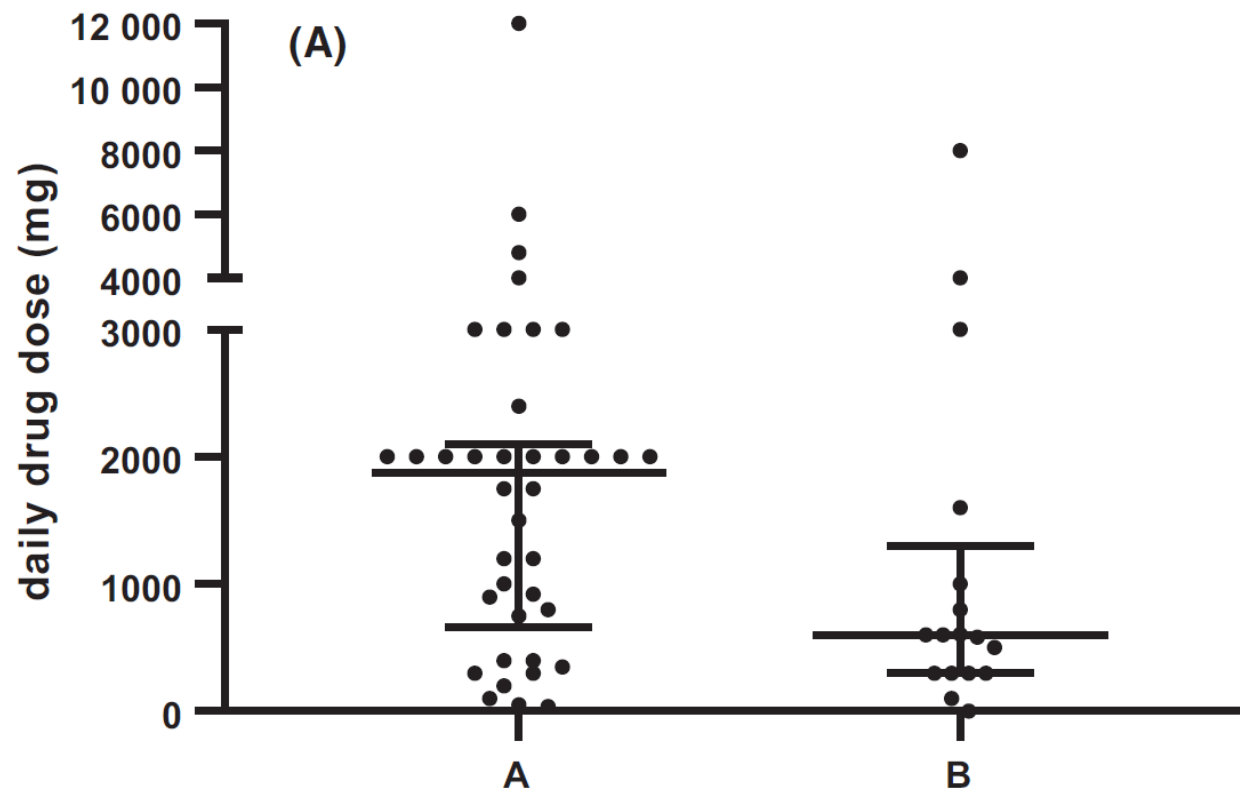
Cytokine profile in case 1 compared to a sequential MDH



DRESS and what follows?

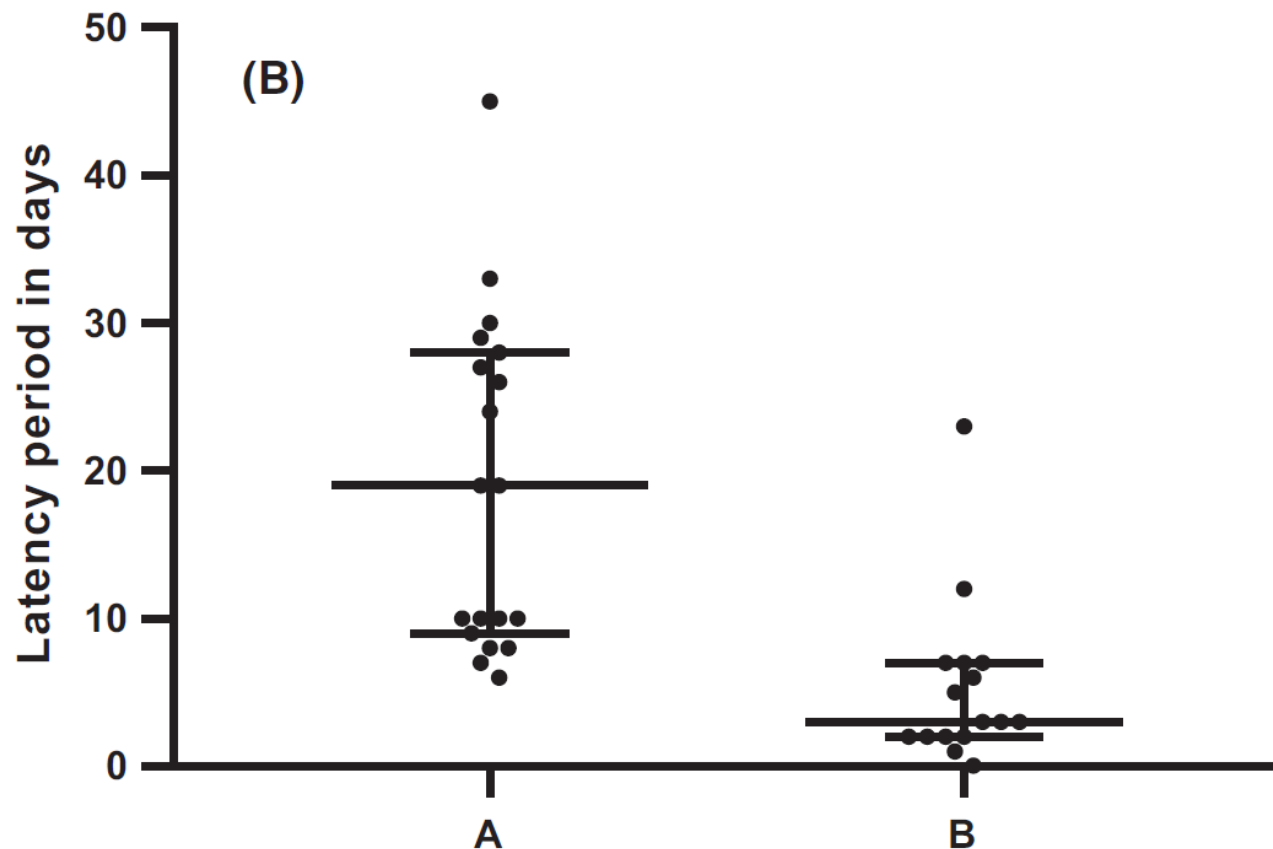


The role of drug dose



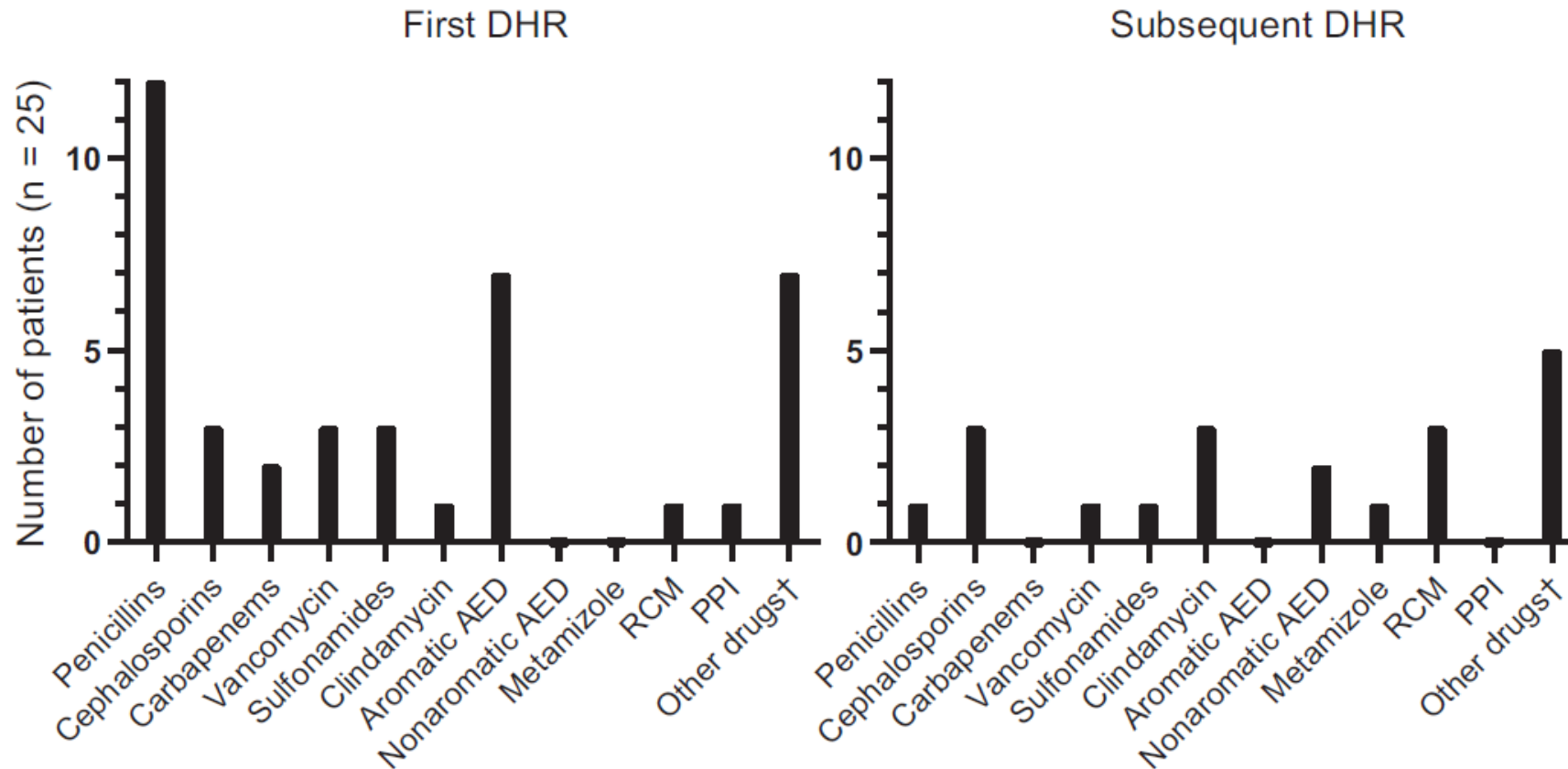
Jörg L, et al. The role of drug, dose, and the tolerance/intolerance of new drugs in multiple drug hypersensitivity syndrome. *Allergy*. 2020 May;75(5):1178-1187.

Latency period of MDH



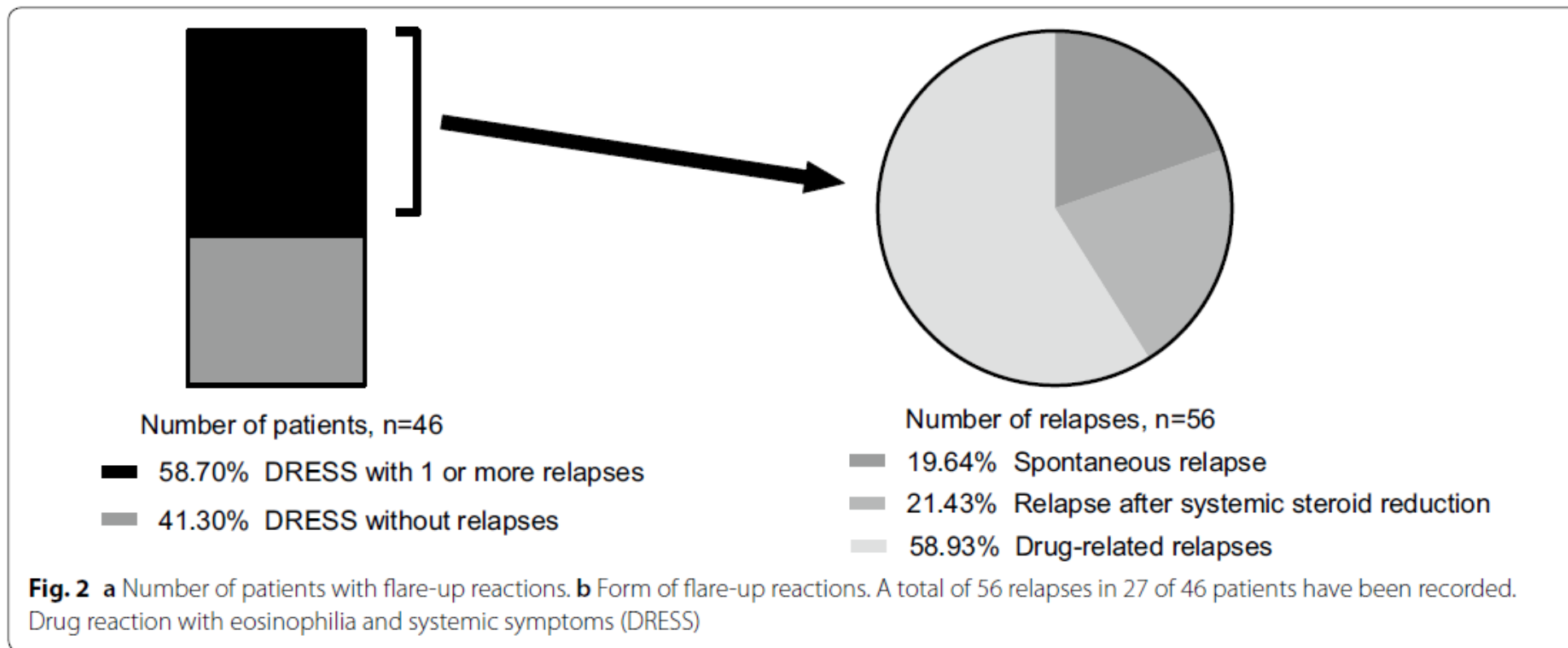
Jörg L, et al. The role of drug, dose, and the tolerance/intolerance of new drugs in multiple drug hypersensitivity syndrome. *Allergy*. 2020 May;75(5):1178-1187.

Which drugs are involved in MDH?



Jörg L, et al. The role of drug, dose, and the tolerance/intolerance of new drugs in multiple drug hypersensitivity syndrome. Allergy. 2020 May;75(5):1178-1187.

Is MDH a result of relapses?



Jörg L, et al. Drug-related relapses in drug reaction with eosinophilia and systemic symptoms (DRESS). Clin Transl Allergy. 2020 Nov 23;10(1):52.

Outlook

Why do some DRESS patients develop MDH and others do not?

Ongoing 4 arm study:

DRESS without MDH

DRESS / MDH

MPE without MDH

Healthy controls

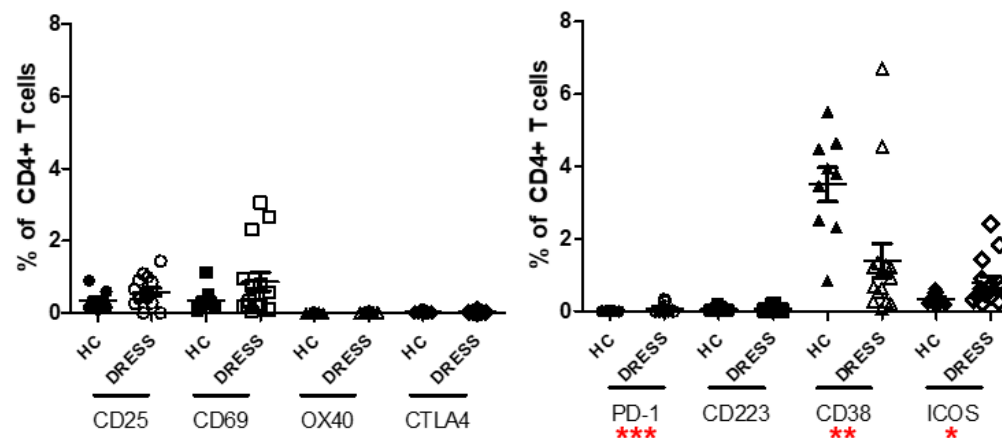
Clinical presentation

Cyto-LTT

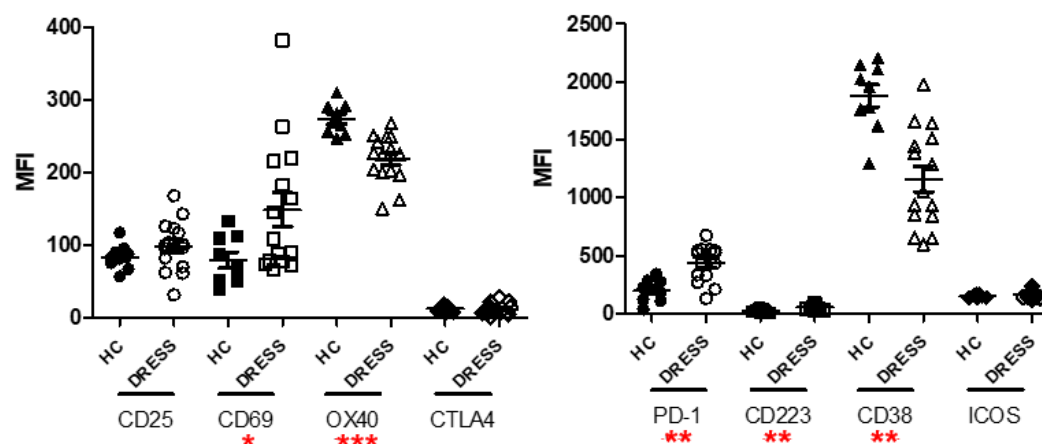
T-cell phenotype

CD4 T-cell phenotype (healthy vs. DRESS)

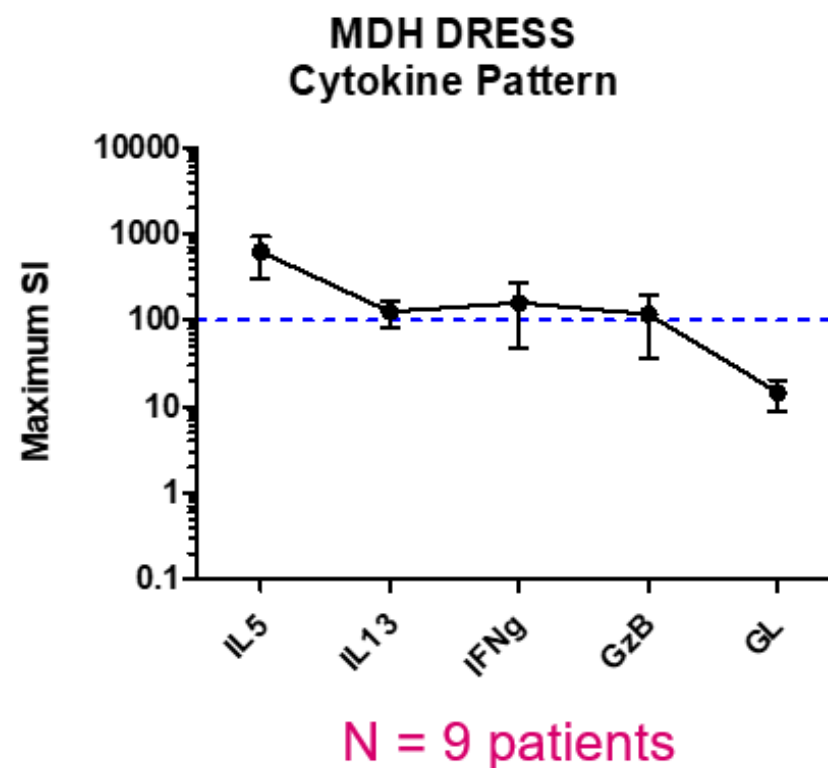
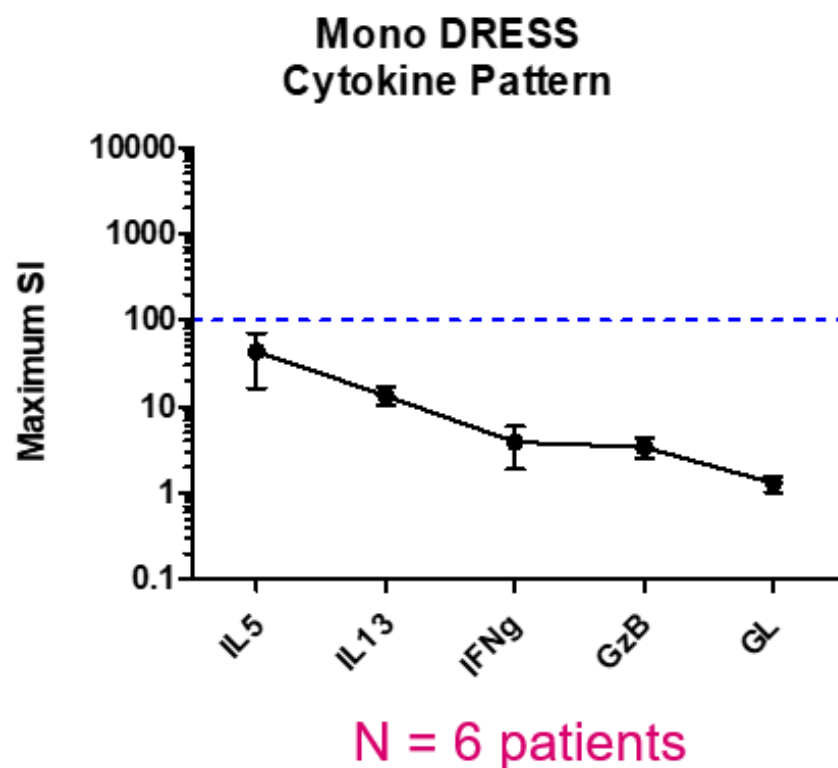
Percentage
positive in CD4



Median
Fluorescence
Intensity in
CD4



IL-5 is the dominant cytokine in DRESS and DRESS/MDH



Summary

Severe DHR, especially DRESS have a high probability to develop MDH

Subsequent DHR in MDH are often MPE

Antibiotics and high dose drugs are most often involved

Flare-up reactions/relapses can be precursor of MDH

DRESS without MDH und with MDH are probably the same phenotype

Thank you for your attention.

