IVIG therapy and hypersensitivity: *the chameleon of infusion reactions*

ZENTRUM FÜR HAUTERKRANKUNGEN

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Introduction:

Intravenous immunoglobulin therapy (IVIG) is a cornerstone of treatment for immune-mediated diseases and is generally well tolerated. Adverse reactions nevertheless occur in a relevant share of infusions, and both **true allergic** and **non-allergic hypersensitivity** reactions contribute.

The **Gell and Coombs** scheme (Types I–IV) can be applied. Alongside IgE-mediated mechanisms, immune complex reactions, direct complement activation and T-cell-mediated hypersensitivity are all relevant**. Latency and clinical appearance is the key discriminator** at the bedside — and the axis along which this series is read.

5-15%

of infusions are accompanied by side effects

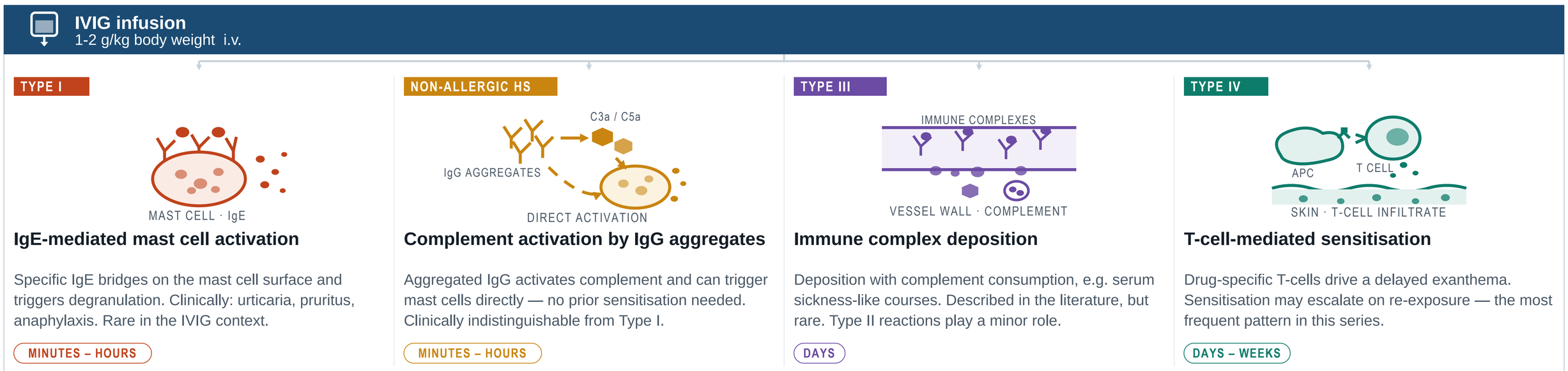


Figure 1: Immunological routes of IVIG-associated reactions. Colour coding by reaction type is carried through the whole poster.

Case reports: six Patients, six Phenotypes

	PATIENT	INDICATION	IVIG	ONSET	PRESENTATION	CLASSIFICATION
1	62 y,m	Distal-predominant sensorimotor polyneuropathy	2 g/kg — first administration	≈ 2 h after start	Generalised pruritus with urticaria	**Grade I anaphylaxis** TYPE I DD non-allergic hypersensitivity
2	88 y,f	Immune-mediated necrotising myopathy	1 g/kg 2023–2024; reinduction 2026	A few hours after start of reinduction	Flushing with globus sensation	**Grade II anaphylaxis** TYPE I DD non-allergic hypersensitivity
3	70 y,m	Multifocal motor neuropathy	2 g/kg — 2 infusions	Days after dose 1; 1 week after dose 2	Mild maculopapular exanthema, then pronounced maculopapular, partly urticarial exanthema	**Drug-induced exanthema with immediate-type urticarial component** TYPE I / IV
4	53 y,m	Sensorimotor axonal demyelinating polyneuropathy	2 g/kg — first administration	≈ 2 weeks after first dose	Disseminated erythrosquamous, itchy plaques	**Immune-mediated psoriasiform / eczematous dermatitis** TYPE IV, HISTOLOGICALLY CONFIRMED
5	78 y,m	Inflammatory neuropathy	2 g/kg — 3 cycles over 3 months	2 weeks after last dose	Macular exanthema	**Drug-induced exanthema** TYPE IV
6	77 y,f	Immunoglobulin deficiency in B-cell lymphoma	n.a.— 5 cycles over 5 months	3 weeks after 5th dose	Macular exanthema	**Drug-induced exanthema** TYPE IV, HISTOLOGICALLY CONFIRMED

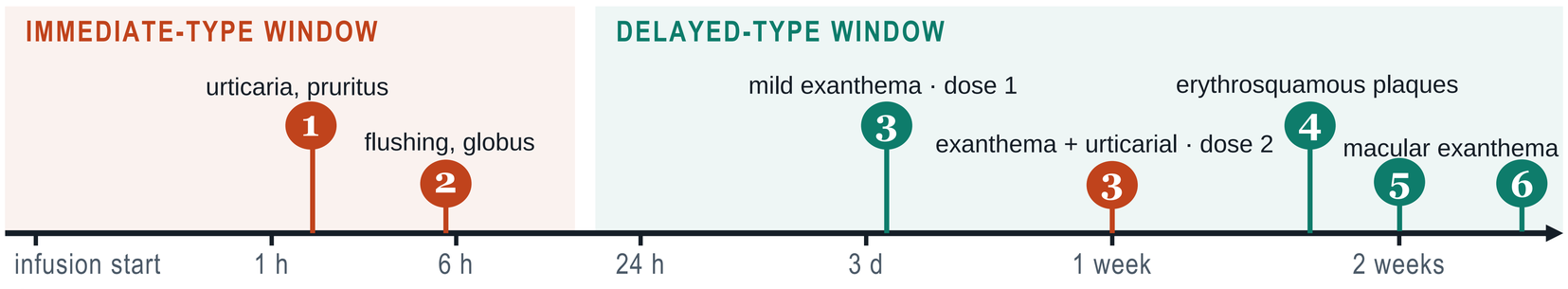


Figure 2: All six cases plotted on a single time axis. Case 3 appears twice: once per exposure.

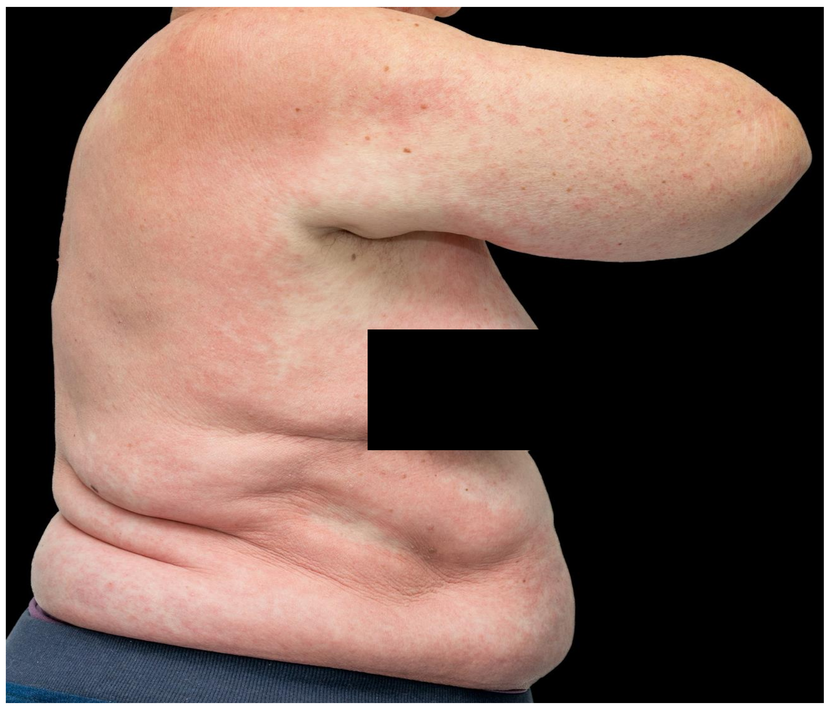


Figure 3: Case 6, clinical appearance

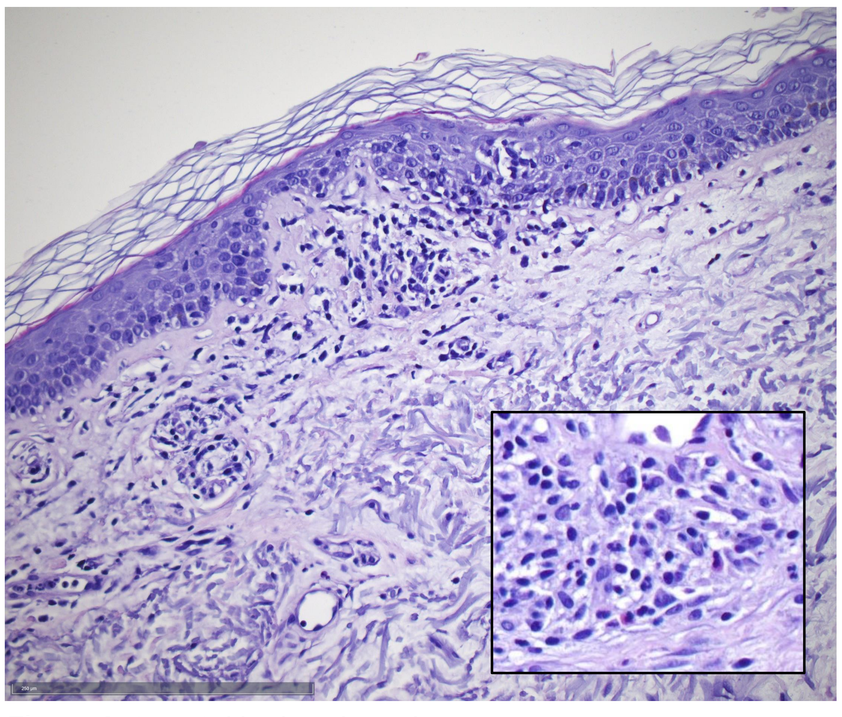


Figure 4: Case 6, histology, he-stain
Characteristic spongiosis with intraepidermal vesicle formation; inset: eosinophilic granulocytes at higher magnification

Results: Workup & Management

IMMEDIATE REACTIONS · TYPE I AND NON-ALLERGIC

Acute reactions occur within minutes to hours of infusion onset and may reflect **IgE-mediated** or, more commonly, **non-allergic mast cell/complement activation**. Management includes acute anaphylaxis treatment and, if life-threatening, cardiopulmonary stabilisation. Subsequent **allergological provocation and avoidance testing** support risk stratification for further infusions.

DELAYED REACTIONS · TYPE IV

Typically presenting as exanthema 1-2 weeks after infusion, Type IV reactions are **T-cell-mediated** and may escalate upon re-exposure. **Epicutaneous patch testing and lymphocyte transformation testing** can provide diagnostic guidance for further treatment.

OTHER REACTIONS & DIFFERENTIAL DIAGNOSIS

Type III reactions (e.g. serum sickness-like courses) are rare, while Type II reactions play a minor role. The broad spectrum of infusion-associated adverse drug reactions should be considered in the differential diagnosis, as these may mimic allergic complications.

Conclusion:

The diverse clinical presentation of IVIG reactions makes them true clinical chameleons, highlighting the importance of accurate classification for safe and effective management. Classification by reaction type (I–IV) is crucial for determining the course of action and further diagnosis. Permanent discontinuation is rarely necessary. Where no alternative preparation exists, structured desensitisation or premedication may be considered. Rapid diagnosis and interdisciplinary collaboration between allergology, dermatology and other involved specialties are essential.

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Literature:
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