

★ IMMUNOLOGY • NGN NCLEX 2026

Hypersensitivity Reactions

Types I, II, III & IV — Mechanisms, Management, Complications & Teaching

Type I: Anaphylactic

Type II: Cytotoxic

Type III: Immune Complex

Type IV: Delayed

1 Definition & Overview

Hypersensitivity = an exaggerated, harmful immune response to an antigen the body has been previously sensitized to. Reactions are classified by the **Gell & Coombs system** into four types based on mechanism and timing. Recognizing the type tells you what to expect, what to do first, and what kills the patient.



Master Mnemonic: A • C • I • D

A

Allergic / Anaphylactic

Type I — IgE

C

Cytotoxic

Type II — IgG / IgM

I

Immune Complex

Type III — Antigen-Antibody

D

Delayed

Type IV — T cells

TYPE I

Anaphylactic / Immediate

IGE • MAST CELLS • HISTAMINE

⌚ Onset: Seconds to minutes

Allergens cross-link IgE on mast cells → massive histamine release → vasodilation, bronchoconstriction, edema.

TYPE II

Cytotoxic

IGG / IGM • COMPLEMENT

⌚ Onset: Minutes to hours

Antibodies bind antigens on cell surfaces → complement-mediated cell destruction (often blood cells).

TYPE III

Immune Complex

ANTIGEN-ANTIBODY COMPLEXES

⌚ Onset: Hours to weeks

Soluble immune complexes deposit in tissue → complement activation → vasculitis, glomerulonephritis.

TYPE IV

Delayed / Cell-Mediated

T LYMPHOCYTES • CYTOKINES

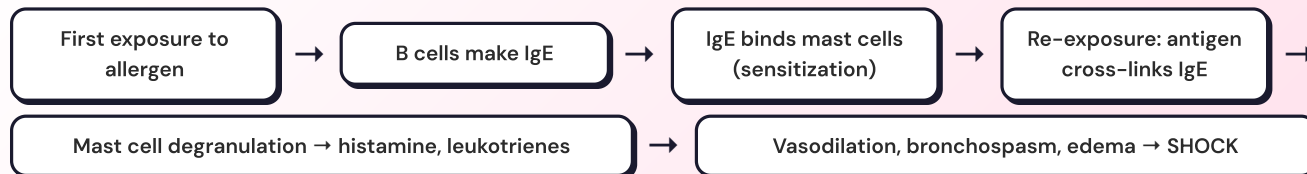
⌚ Onset: 24–72 hours

Sensitized T cells release cytokines → macrophage activation → local inflammation. **No antibodies.**

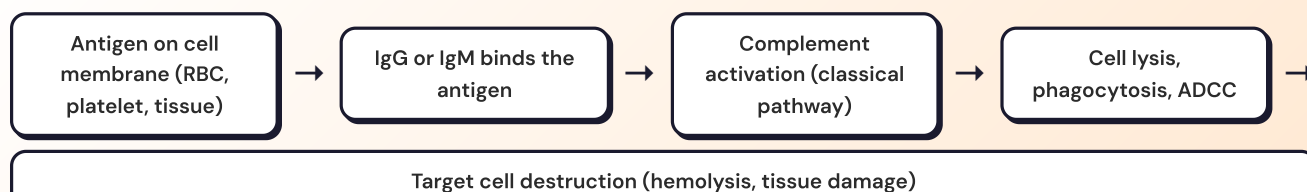
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Pathophysiology — Step by Step

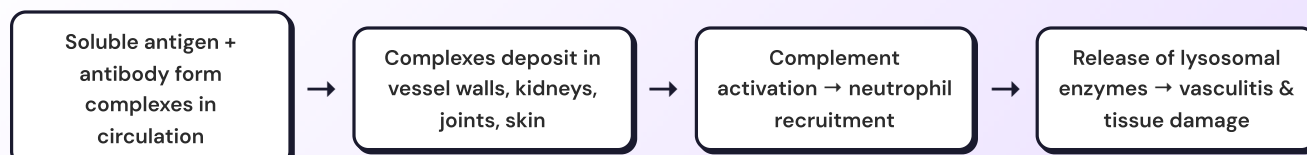
♥ Type I — IgE-Mediated Cascade



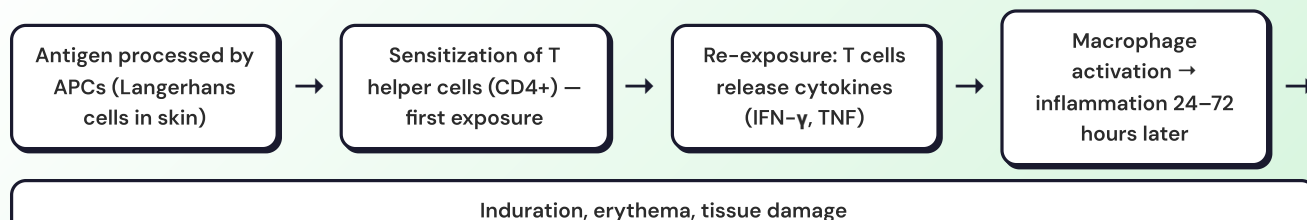
♥ Type II — Cytotoxic Cascade



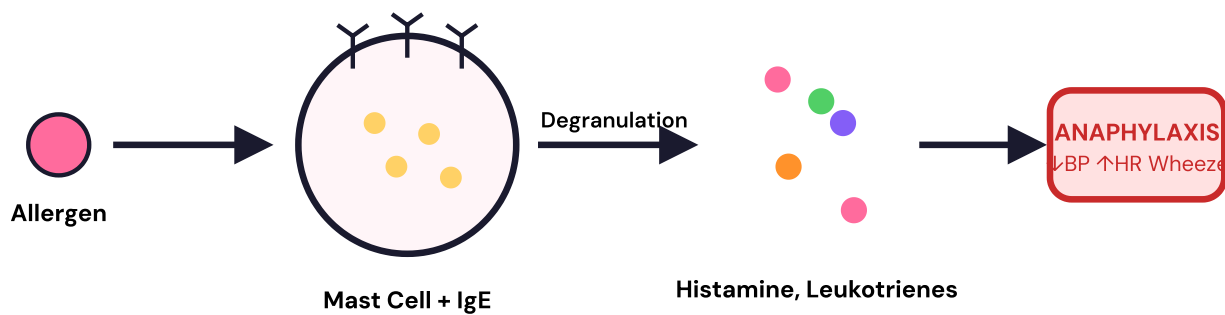
♥ Type III — Immune Complex Deposition



♥ Type IV — T Cell-Mediated Delayed Reaction



Mast Cell Degranulation (Type I)





Type I — Anaphylactic / Immediate Hypersensitivity

"The IgE explosion — minutes to disaster"

COMMON TRIGGERS

- Peanuts/tree nuts
- Bee stings
- Penicillin
- Latex
- Shellfish
- Eggs
- IV contrast
- Pollen

CLINICAL EXAMPLES

- **Anaphylaxis** (life-threatening)
- Allergic rhinitis / hay fever
- Allergic asthma
- Atopic dermatitis (eczema)
- Urticaria (hives) & angioedema
- Food allergies

⚠️ Early / Mild S&S

- Itching, flushing, warmth
- Urticaria (hives)
- Sneezing, rhinorrhea, watery eyes
- Tingling lips/tongue
- Anxiety, "sense of doom"
- Mild GI upset, nausea

🚑 Severe / Anaphylaxis

- **Stridor, wheezing, throat tightness**
- **Angioedema** (lips, tongue, face)
- **Hypotension, tachycardia**
- Bronchospasm, dyspnea
- Loss of consciousness, shock
- Cardiac/respiratory arrest

🚑 RED FLAG — Anaphylaxis Triad

Airway compromise + Hypotension + Skin signs (urticaria/angioedema) = call rapid response NOW. Epinephrine first — do NOT delay for IV access or other meds.

💊 Management (Anaphylaxis Protocol)

1. **Epinephrine 0.3–0.5 mg IM** (1:1000) — vastus lateralis, repeat q5–15 min PRN
2. **Maintain airway** — O₂ 100%, prepare for intubation/cricothyrotomy
3. **Position supine, legs elevated** (Trendelenburg) if hypotensive
4. **IV NS bolus** 1–2 L for hypotension
5. Diphenhydramine 25–50 mg IV/IM (H1 blocker)
6. Ranitidine/famotidine IV (H2 blocker, adjunct)
7. Methylprednisolone IV (prevents biphasic reaction)
8. Albuterol nebulizer for bronchospasm
9. Observe 4–6 hours minimum (biphasic risk up to 72 hrs)

⚠️ Complications

Biphasic reaction (return of symptoms 1–72 hrs later), prolonged hypotension, hypoxic brain injury, death from airway obstruction or cardiovascular collapse.

🎓 Patient Teaching

- **Strict trigger avoidance** — read all labels, ask in restaurants
- Carry **2 EpiPens at all times**; demonstrate use, check expiration monthly
- Inject through clothing into outer thigh, hold 10 seconds, call 911 after use

- Wear **MedicAlert bracelet**
- Inform all healthcare providers of allergies
- Allergy testing referral, consider immunotherapy



Type II — Cytotoxic Hypersensitivity

"Antibodies attacking your own cells"

CLINICAL EXAMPLES

- **Hemolytic transfusion reaction** (ABO mismatch)
- **Hemolytic disease of the newborn** (Rh incompatibility)
- Autoimmune hemolytic anemia
- Idiopathic thrombocytopenic purpura (ITP)
- Goodpasture syndrome (lung & kidney)
- Myasthenia gravis (anti-ACh receptor)
- Graves disease (anti-TSH receptor)
- Drug-induced hemolytic anemia

MECHANISM RECAP

Antibodies (IgG or IgM) bind antigens on cell surfaces → activate complement → cell lysis OR opsonization for phagocytosis. The "target" is usually a blood cell or tissue cell.

⚠️ Hemolytic Transfusion S&S

- **Low back/flank pain** (classic!)
- Chills, fever (early)
- Hypotension, tachycardia
- Flushing, tachypnea
- Hemoglobinuria (dark urine)
- Sense of impending doom

🚑 Severe / DIC

- **Acute kidney injury**
- **DIC** (bleeding, clotting)
- Jaundice (hemolysis)
- Shock, cardiovascular collapse
- Multi-organ failure

🚑 RED FLAG — Transfusion Reaction

Low back pain during transfusion = hemolytic until proven otherwise. Stop the transfusion **FIRST**, then NS via NEW tubing, notify HCP & blood bank, send blood + urine sample.

💊 Management

1. **Stop the offending agent immediately** (transfusion, drug)
2. Maintain IV access with NS (new tubing for transfusion reaction)
3. Support BP, oxygenation, urine output
4. Send blood bag + tubing + blood/urine samples to lab
5. Immunosuppressants (steroids, rituximab) for autoimmune forms
6. Plasmapheresis for severe cases (myasthenia, Goodpasture)
7. IVIG for ITP
8. RhoGAM for Rh-negative pregnancy prophylaxis

⚠️ Complications

Acute renal failure from hemoglobin damage, DIC, severe anemia, shock, organ-specific damage (muscle weakness, kidney failure, thyroid storm).

🎓 Patient Teaching

- Importance of type & crossmatch verification — two nurse check
- Report low back pain, chills, fever, dark urine immediately during transfusion

- Rh-negative pregnant women: receive RhoGAM at 28 weeks and within 72 hrs of delivery
- Autoimmune disease management: medication adherence, monitor labs, infection precautions



Type III — Immune Complex Hypersensitivity

"Complexes deposit, complement activates, tissue burns"

CLINICAL EXAMPLES

- **Systemic Lupus Erythematosus (SLE)**
- Rheumatoid arthritis (RA)
- **Serum sickness**
- Post-streptococcal glomerulonephritis
- Hypersensitivity pneumonitis ("farmer's lung")
- Arthus reaction (localized)
- Polyarteritis nodosa

MECHANISM RECAP

Soluble antigen + antibody form complexes circulating in the bloodstream → lodge in small vessels of joints, kidneys, skin, lungs → complement activation → neutrophils swarm → enzymes destroy local tissue.

⚠️ Early S&S (1–3 wks post-trigger)

- Fever, malaise, fatigue
- Joint pain (arthralgia)
- Skin rash, urticaria, purpura
- Lymphadenopathy
- Headache

🚑 Severe / Organ Damage

- **Glomerulonephritis** (hematuria, proteinuria, ↑BUN/Cr)
- **Vasculitis** with skin necrosis
- Pulmonary infiltrates
- Pericarditis, pleurisy
- SLE: butterfly rash, photosensitivity, oral ulcers

🚑 RED FLAG — Renal Involvement

Hematuria + edema + hypertension 1–3 weeks after strep throat = post-streptococcal glomerulonephritis. Monitor I&O, BP, daily weight, BUN/creatinine.

💊 Management

1. Remove/treat the inciting antigen (treat infection, stop drug)
2. **NSAIDs** for joint pain and inflammation
3. **Corticosteroids** (prednisone, methylprednisolone) — first-line for moderate-severe
4. **Immunosuppressants**: hydroxychloroquine, methotrexate, cyclophosphamide, azathioprine
5. Biologics: rituximab, belimumab for refractory SLE/RA
6. **Plasmapheresis** for severe cases (removes circulating complexes)
7. Dialysis if renal failure develops
8. Monitor renal function, urinalysis, complement levels (C3, C4)

⚠️ Complications

Chronic kidney disease, end-stage renal disease, joint deformity, pericarditis/myocarditis, neurologic involvement (lupus cerebritis), increased infection risk from immunosuppression.

🎓 Patient Teaching

- **SLE: avoid sun exposure** — use SPF 30+, hats, long sleeves (UV triggers flares)
- Medication adherence — never abruptly stop steroids/immunosuppressants
- Infection prevention: hand hygiene, vaccines (avoid live), avoid sick contacts
- Report signs of flare: rash, joint pain, fever, fatigue, foamy/dark urine

- Regular labs: CBC, BUN/Cr, urinalysis, complement, ANA
- Stress, infection, pregnancy, fatigue trigger flares

IV

Type IV — Delayed (Cell-Mediated) Hypersensitivity

"T cells take their time — no antibodies needed"

CLINICAL EXAMPLES

- **TB skin test (PPD/Mantoux)** — read 48–72 hrs
- **Contact dermatitis** (poison ivy, nickel, latex chronic)
- **Transplant rejection** (acute & chronic)
- Graft-versus-host disease (GVHD)
- Type 1 Diabetes Mellitus
- Multiple sclerosis
- Hashimoto thyroiditis
- Crohn disease

KEY DISTINGUISHING FEATURES

- **No antibodies, no histamine**
- Reaction is **delayed 24–72 hours**
- Mediated entirely by T lymphocytes
- Hallmark sign: **induration** (firm raised area), not just redness
- Granuloma formation in chronic cases (TB, sarcoidosis)

⚠️ Contact Dermatitis S&S

- Erythema (redness) at contact site
- **Pruritus** (itching) — intense
- Vesicles, papules, weeping
- Edema, scaling
- Linear pattern with poison ivy

🚑 Transplant Rejection S&S

- Fever, malaise
- Pain/tenderness over graft site
- Organ-specific dysfunction (↓UO for kidney, dyspnea for lung)
- Elevated organ markers (creatinine, LFTs)
- Acute: days–months post-transplant

🚑 RED FLAG — Reading the PPD

Read the TB skin test **48–72 hours after placement**. Measure **INDURATION** (firm raised area), NOT erythema. Positive cutoffs: ≥5 mm (HIV/immunocompromised), ≥10 mm (high-risk groups), ≥15 mm (low-risk).

💊 Management

1. **Remove/avoid the trigger** — wash skin, remove jewelry, change products
2. **Topical corticosteroids** (hydrocortisone, triamcinolone) for contact dermatitis
3. Cool compresses, calamine, oatmeal baths for pruritus
4. Oral antihistamines (Benadryl) for itch (note: less effective than in Type I)
5. Systemic corticosteroids for severe/widespread reactions
6. **Transplant rejection**: high-dose IV steroids, calcineurin inhibitors (cyclosporine, tacrolimus), mycophenolate, antithymocyte globulin
7. Lifelong immunosuppression post-transplant

⚠️ Complications

Chronic dermatitis, secondary bacterial infection from scratching, graft loss, opportunistic infections from immunosuppression (CMV, PCP, fungal), increased malignancy risk (skin cancer, PTLD).

🎓 Patient Teaching

- **Return for PPD reading in 48–72 hours** — measure induration only
- Identify and avoid contact triggers — patch testing if unsure

- Wear gloves when handling known irritants; wash skin within 10 minutes of exposure
- Don't scratch — risks infection; trim nails short
- **Post-transplant:** lifelong immunosuppression, infection precautions, report fever/graft pain/↓function immediately
- Avoid live vaccines while immunosuppressed

3 Quick Comparison Table

TYPE	ONSET	MEDIATOR	HALLMARK	CLASSIC EXAMPLE	TREATMENT
I Anaphylactic	Seconds–min	IgE, mast cells, histamine	Wheeze + ↓BP + hives	Anaphylaxis, asthma, hay fever	Epinephrine IM , O ₂ , antihistamines, steroids
II Cytotoxic	Min–hours	IgG/IgM, complement	Cell destruction (esp. blood)	Hemolytic transfusion reaction, Goodpasture	Stop trigger , NS, support, immunosuppression
III Immune Complex	Hours–weeks	Ag–Ab complexes	Vasculitis, GN, joint pain	SLE, RA, serum sickness, PSGN	NSAIDs, steroids , immunosuppressants
IV Delayed	24–72 hrs	T cells, cytokines	Induration, granuloma	PPD test, contact dermatitis, transplant rejection	Avoid trigger, topical/systemic steroids

4 Priority Nursing Interventions — ABC Framework

A

AIRWAY

- Assess for stridor, hoarseness, tongue/lip edema
- Prepare for intubation / cricothyrotomy
- Position upright if alert
- Suction PRN

B

BREATHING

- Apply O₂ 100% via NRB
- Auscultate lungs — wheezing? crackles?
- Continuous SpO₂ monitoring
- Albuterol nebulizer for bronchospasm

C

CIRCULATION

- Continuous BP, HR, ECG
- **2 large-bore IVs**, NS bolus 1–2 L
- Trendelenburg if hypotensive
- Epinephrine IM for anaphylaxis

Universal Priority Steps (any suspected hypersensitivity)

1. **STOP the trigger immediately** — transfusion, drug infusion, food, contact agent
2. **Assess ABCs and call for help / rapid response**
3. **Maintain IV access** with 0.9% NS — use new tubing for transfusion reactions
4. **Administer emergency meds per protocol** — Epi first for anaphylaxis
5. Notify HCP and (if transfusion) blood bank
6. Send blood + urine samples to lab if hemolytic reaction suspected
7. Document time of onset, symptoms, interventions, and patient response
8. **Stay with the patient** — DO NOT leave during acute reaction
9. Monitor for biphasic reaction (Type I) for up to 72 hours
10. Update allergy list, MAR, and chart prominently

5 Pharmacology — Key Medications

DRUG / CLASS	USE	MECHANISM	NURSING CONSIDERATIONS
Epinephrine (1:1000)	Anaphylaxis — Type I	α & β agonist; vasoconstriction, bronchodilation	FIRST drug given. 0.3–0.5 mg IM vastus lateralis. Repeat q5–15 min. Monitor HR/BP, tachycardia expected. Refrigerate auto-injectors per package.
Diphenhydramine (Benadryl)	Hives, mild allergic reaction, adjunct in anaphylaxis	H1 receptor blocker — blocks histamine	Causes drowsiness, dry mouth, urinary retention. Avoid in elderly (anticholinergic). NOT first line for anaphylaxis.
Famotidine / Ranitidine	Adjunct for anaphylaxis, urticaria	H2 receptor blocker — blocks histamine on parietal cells & vascular	Synergistic with H1 blockers; given IV with Benadryl.
Methylprednisolone / Prednisone	All hypersensitivity types	Anti-inflammatory; suppresses immune response	Prevents biphasic reaction (Type I). Monitor blood glucose, BP, infection signs. Never abruptly stop. Long-term: osteoporosis, weight gain, cataracts.
Albuterol (nebulizer)	Bronchospasm (Type I)	β_2 agonist — bronchodilation	May cause tachycardia, tremor, anxiety. Monitor HR & response.
Hydroxychloroquine (Plaquenil)	SLE, RA — Type III	Disease-modifying antirheumatic (DMARD)	Risk of retinal toxicity — annual eye exams. Takes weeks to months for effect.
Methotrexate	RA, severe psoriasis — Type III	Folic acid antagonist; immunosuppressant	Teratogenic — pregnancy contraindicated. Monitor LFTs, CBC. Give with folic acid. Avoid alcohol.
Cyclosporine / Tacrolimus	Transplant rejection — Type IV	Calcineurin inhibitor; suppresses T cells	Monitor trough levels, BUN/creatinine (nephrotoxic). Hypertension, tremor, gingival hyperplasia.
Topical Hydrocortisone	Contact dermatitis — Type IV	Local anti-inflammatory	Thin layer 2–3x daily. Avoid prolonged use on face (skin atrophy).
RhoGAM (Rh immune globulin)	Prevent Rh hemolytic disease of newborn — Type II	Anti-D antibody; prevents maternal sensitization	Rh-negative mom: 28 weeks gestation + within 72 hrs of delivery/miscarriage/amnio.

6 NCLEX Test Traps ⚠️

❌ Wrong Answer Patterns

- Giving **Benadryl** first for anaphylaxis
- Starting an IV before giving epinephrine
- Reading a TB skin test by measuring **redness**
- Reading the PPD at 24 hours
- Continuing transfusion while "checking" reaction
- Restarting the same blood unit after reaction
- Giving epinephrine subcutaneously instead of IM
- Treating contact dermatitis with epinephrine
- Stopping immunosuppressants abruptly
- Giving live vaccines to immunosuppressed transplant patient

✅ Right Answer Patterns

- **Epinephrine IM** — FIRST for anaphylaxis
- **Stop transfusion** — FIRST for hemolytic reaction
- Measure **induration** for TB skin test
- Read PPD at **48–72 hours**
- Use **new tubing** with NS after transfusion stop
- Maintain airway, then circulation
- **Vastus lateralis** for epi injection
- Wash skin within 10 min of contact allergen
- Taper steroids gradually
- **Avoid live vaccines** in immunosuppressed

🎯 Top NCLEX Discriminators

"What's the **FIRST** action?" for anaphylaxis → **Epinephrine IM** (not Benadryl, not IV, not call HCP)

"What's the **FIRST** action?" for transfusion reaction → **Stop the transfusion** (not call HCP, not slow rate)

"**Low back pain during transfusion**" = hemolytic reaction (Type II) — STOP NOW

"**Hives + wheezing + ↓BP**" = Type I anaphylaxis

"**Butterfly rash + joint pain + ↑BUN**" = Type III (SLE)

"**Itchy rash on wrist where watch sits**" = Type IV (contact dermatitis to nickel)

7 Patient & Family Education



EpiPen Use (Type I)

- Carry **two** auto-injectors at all times
- Inject into **outer thigh** through clothing if needed
- Hold in place for **10 seconds**
- Call 911 immediately after use — go to ER even if symptoms resolve
- Check expiration date monthly; solution should be clear
- Store at room temperature; do not refrigerate or leave in hot car
- Family members & caregivers must know how to use it



Trigger Avoidance

- Read **every food label**; ask in restaurants about cross-contamination
- Wear **MedicAlert bracelet** at all times
- Inform all healthcare providers, dentists, employers, schools
- Avoid known triggers: insects, drugs, latex, foods, contact agents
- Patch testing for unidentified contact allergens (Type IV)
- Carry emergency action plan written by HCP



SLE Self-Care (Type III)

- Avoid sun — SPF 30+, hats, long sleeves (UV triggers flares)
- Take all medications as prescribed; never stop steroids abruptly
- Recognize flare signs: rash, joint pain, fever, fatigue, foamy/dark urine
- Manage stress, get adequate sleep, balanced diet
- Regular labs: CBC, BUN/Cr, urinalysis, complement, ANA
- Pregnancy planning with rheumatology — flares common postpartum



Contact Dermatitis (Type IV)

- Wash skin with mild soap & water **within 10 minutes** of contact
- Apply topical hydrocortisone, cool compresses, calamine
- Avoid scratching — trim nails short, wear cotton gloves at night
- Identify and remove offending agent (jewelry, plant, product)
- Wear protective clothing/gloves when exposure is unavoidable
- "Leaves of three, let it be" — poison ivy/oak/sumac



Transfusion Patient (Type II)

- Report **any** new symptom during transfusion immediately: back pain, chills, fever, itching, SOB
- Two nurses verify blood unit at bedside before infusion
- Vital signs before, at 15 min, then per protocol
- Stay near call light; do not leave room first 15 min
- Rh-negative pregnancy: RhoGAM at 28 wks + within 72 hrs of delivery



Post-Transplant (Type IV)

- Take immunosuppressants on schedule — lifelong commitment
- Report any fever, graft pain, ↓function (UO, dyspnea) immediately
- Avoid **live vaccines** (MMR, varicella, live flu)
- Infection precautions: hand hygiene, sick contacts, raw foods, pet feces
- Annual skin exams (↑ skin cancer risk)
- Avoid grapefruit (interacts with calcineurin inhibitors)

8

Memory Boosters & Mnemonics

A · C · I · D

THE 4 TYPES IN ORDER

- Allergic / Anaphylactic — Type I
- Cytotoxic — Type II
- Immune complex — Type III
- Delayed — Type IV

1 · 2 · 3 · 4

TIMING BY TYPE

- Type 1: 1 minute (immediate)
- Type 2: minutes to hours
- Type 3: hours to weeks (build-up)
- Type 4: 48 hours+ (delayed)

"WHEAL"

ANAPHYLAXIS SIGNS

- Wheezing
- Hives
- Edema (angioedema, tongue/throat)
- Anxiety / sense of doom
- Low BP

"SOAP"

ANAPHYLAXIS TREATMENT

- Stop trigger / Stay with patient
- Oxygen 100% NRB
- Adrenaline (Epinephrine IM)
- Positioning supine, legs elevated

"ABCDE"

TYPE II CYTOTOXIC DISEASES

- Autoimmune hemolytic anemia
- Blood transfusion reaction
- Coombs-positive (drug-induced)
- Down with Rh (HDN)
- Everything with anti-cell antibodies

"SHARP"

TYPE III DISEASES

- SLE (Lupus)
- Hypersensitivity pneumonitis
- Arthus reaction
- Rheumatoid arthritis
- Post-strep glomerulonephritis

"4 T's"

TYPE IV REACTIONS

- Tuberculin (PPD) skin test
- Touching (contact dermatitis)
- Transplant rejection
- T-cells mediate them all

"I·G·G·T"

MEDIATOR BY TYPE

- Type I → IgE
- Type II → IgG/IgM (cells)
- Type III → IgG/IgM (complexes)
- Type IV → T cells

9 NCJMM Clinical Judgment Scenario

Scenario

A 28-year-old client with a peanut allergy arrives at the ED 20 minutes after eating a granola bar at work. They report rapidly worsening throat tightness, difficulty breathing, and feeling "like something terrible is happening." Vital signs: BP 82/48, HR 138, RR 28, SpO₂ 86% on room air, T 98.4°F. The nurse notes diffuse urticaria, audible wheezing, swollen lips, and the client speaking in 2–3 word sentences.

1

RECOGNIZE CUES

Critical cues: Throat tightness, wheezing, urticaria, lip swelling (angioedema), BP 82/48 (hypotension), HR 138 (tachycardia), SpO₂ 86% (hypoxia), sense of doom, recent peanut exposure.

2

ANALYZE CUES

This pattern = **Type I IgE-mediated anaphylaxis**. Known allergen + airway/breathing/circulation triad. Mast cell degranulation → histamine → bronchospasm + vasodilation + capillary leak.

3

PRIORITIZE HYPOTHESIS

#1 priority: Anaphylactic shock with imminent airway loss & cardiovascular collapse. Differential ruled out: not pneumonia (no fever, rapid onset), not cardiac (skin findings + allergen trigger).

4

GENERATE SOLUTIONS

Epinephrine 0.3–0.5 mg IM vastus lateralis FIRST. O₂ 100% NRB. Supine + legs elevated. Two large-bore IVs, NS bolus. Benadryl + famotidine IV. Methylprednisolone IV. Albuterol neb. Prepare for intubation.

5

TAKE ACTION

Administer epinephrine immediately (do NOT wait for IV). Call rapid response. Establish IV access × 2. Continuous monitoring (ECG, BP, SpO₂). Stay with the client. Document time of onset and interventions.

6

EVALUATE OUTCOMES

Improving: BP rising, HR ↓, SpO₂ ≥94%, wheezing resolving, edema receding, mental status clearing. **Worsening:** Persistent hypotension → repeat epi q5–15 min. Observe ≥4–6 hours for biphasic reaction.

Diane's NGN NCLEX 2026 Study Series • Hypersensitivity Reactions Types I–IV

Immunology • Pharmacology • Clinical Judgment • Patient Safety