PATHOPHYSIOLOGY · CHAPTER 19

Parts 5 & 6

Disease at the Organ Level

The Body’s Defenses Against Disease and Injury

Paramedic Program · Instructor Presentation with Teaching Notes

Part 5

Disease at the Organ Level

1. Genetics & risk factors
2. Perfusion & the circulatory system
3. Pathophysiology of shock
4. Types of shock
5. MODS

Genetics, Environment, Lifestyle, Age and Gender

Most disease is not one cause — it is a collision of several

The genetic foundation

- Inherited traits are determined by DNA, organized into genes on chromosomes
- Human somatic cells contain 46 chromosomes; sex cells contain 23
- 23 chromosomes come from each parent
- A person cannot change their genetics, gender or age — only lifestyle and environment

Purely genetic vs. multifactorial

Some diseases are purely genetic — sickle cell disease, cystic fibrosis, Huntington disease. Most are multifactorial: a genetic susceptibility that requires an environmental or lifestyle trigger to become disease.

Type 2 diabetes, coronary artery disease and most cancers sit in this second category. Genetics loads the gun; environment pulls the trigger.

Systems where genetics and other risk factors intersect

Immunologic	**Cancer**	**Endocrine**	**Hematologic**	**Cardiovascular**
Renal	**Rheumatic**	**Gastrointestinal**	**Neuromuscular**	**Psychiatric**

Named Disorders by Body System

The conditions behind the categories — where a genetic contribution is established

Systems in which inherited susceptibility is well documented

1 Hematologic

Hemophilia — inherited clotting factor deficiency. Hemochromatosis — iron overload. Anemia.

2 Cardiovascular

Prolonged QT interval. Mitral valve prolapse. Coronary artery disease. Hypertension. Cardiomyopathy.

3 Endocrine

Diabetes mellitus — type 1 and type 2. The single most common endocrine disorder you will encounter.

4 Immunologic

Rheumatic fever. Allergies. Asthma. All three are immune responses running beyond useful limits.

Where a family history changes what you are looking for

1 Gastrointestinal

Lactose intolerance. Crohn disease — chronic inflammation of the digestive tract wall. Peptic ulcers. Cholecystitis. Obesity, defined as more than 20 percent over ideal body weight.

Renal failure and gout belong here too: gout deposits crystals in joints, classically the great toe.

2 Neuromuscular

Huntington disease — uncontrollable jerking and writhing movements. Muscular dystrophy — progressive muscle weakness. Multiple sclerosis — nerves of the eye, brain and cord. Alzheimer disease — cause of roughly half of all dementias.

Each one changes the patient's baseline. Ask the caregiver what normal looks like.

3 Psychiatric

Schizophrenia — loss of contact with reality, with hallucinations, delusions, disordered thinking and disrupted social function.

Bipolar disorder, formerly manic-depressive illness — alternating periods of depression and mania.

Both carry a genetic component. Neither is a character failure.

4 Cancer risk

Breast — greatest risk factor is female gender, second is age; a first-degree relative raises risk two to three times.

Colorectal — age and family history; rectal more common in men, colon in women.

Lung — overwhelmingly environmental. Smoking is the main cause, with asbestos, arsenic and nickel usually occupational.

Hypoperfusion

The most important concept in prehospital medicine

Perfusion is the constant and necessary passage of blood through the body's tissues. **Hypoperfusion — shock —** is inadequate perfusion of body tissues. It is progressive and fatal if not corrected.

1 It is not a blood pressure

Blood pressure is a number we can measure. Shock is what is happening in the tissues. A patient can be in shock with a perfectly normal pressure — and often is, early on.

2 Every type shares one endpoint

Cardiogenic, hypovolemic, neurogenic, anaphylactic, septic and obstructive shock have different causes but identical pathophysiology at the cellular and tissue levels.

3 The endpoint is the mitochondrion

Whatever the cause, the result is that cells cannot get or cannot use oxygen. Aerobic metabolism fails, ATP production collapses, and cells begin to die.

The chain to remember: Impaired use of oxygen and glucose → cellular death → tissue death → organ failure → organ system failure → death of the organism. Every intervention we perform on a shock patient is an attempt to interrupt that chain as far to the left as possible.

Components of the Circulatory System

Three parts — and shock is a failure of one or more of them

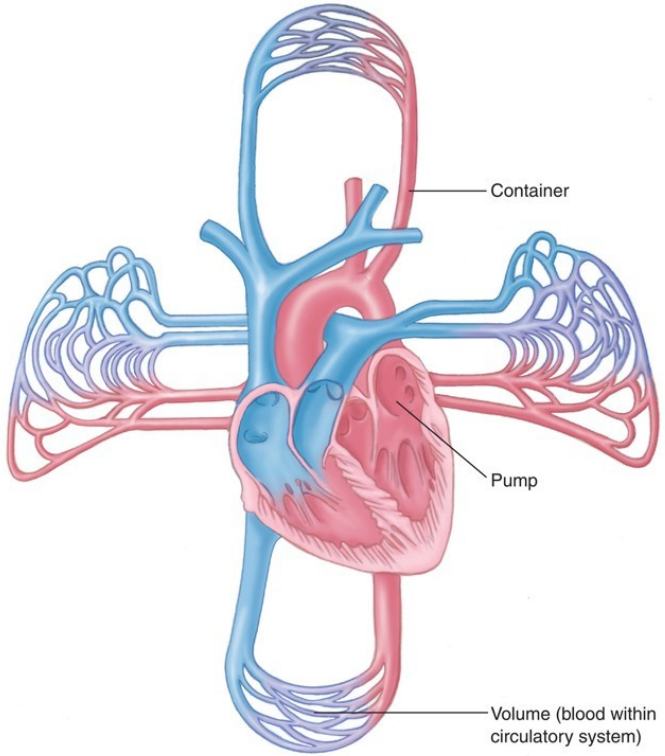

Figure 19-84 Components of the circulatory system

Bledsoe, Porter & Cherry, Paramedic Care: Principles & Practice, 6th ed. © Pearson Education, Inc.

1 The pump

The heart. Generates the pressure that moves blood. Fails in cardiogenic shock — and in obstructive shock, where the pump itself is fine but is being prevented from filling or emptying.

2 The fluid

Blood — plasma plus formed elements. Carries oxygen, carbon dioxide, nutrients, hormones, waste and heat. Lost in hypovolemic and hemorrhagic shock.

3 The container

The blood vessels. Normally holds the volume under tension. Fails in distributive shock — neurogenic, anaphylactic and septic — where the container dilates and the same volume no longer fills it.

Every shock state is a pump problem, a fluid problem, or a container problem.

The Pump

What determines how much blood the heart actually moves

1 Preload

The volume of blood delivered to the heart during diastole — the stretch on the ventricle before it contracts.

More preload means more stretch, and within limits, a stronger contraction (Frank–Starling).

2 Contractility

The inherent strength of the cardiac contraction.

Enhanced by catecholamines; depressed by hypoxia, acidosis, ischemia and certain drugs.

3 Afterload

The resistance the ventricle must contract against.

Determined largely by peripheral vascular resistance. Raise it too far and stroke volume falls.

The equations worth memorizing

Cardiac output = heart rate × stroke volume

Blood pressure = cardiac output × peripheral vascular resistance

Cardiac output is the volume pumped in one minute. Stroke volume is set by preload, contractility and afterload.

Why the blood pressure lies to you

Look at the second equation. If cardiac output falls, the body can hold blood pressure constant by raising peripheral vascular resistance — clamping down the container. That is exactly what a compensating patient does.

So a normal blood pressure in a bleeding patient does not mean adequate output. It means the compensatory mechanisms are still winning. Tachycardia, narrowing pulse pressure and cool skin are the signs that this is happening.

Oxygen Transport and the Fick Principle

Five things must all work — break any one and the cell starves

1

Adequate inspired oxygen

Enough oxygen has to reach the alveoli in the first place.

Fails in: smoke-filled room, altitude, apnea, airway obstruction

2

Movement across the membrane

Oxygen must diffuse across the alveolar-capillary membrane into the blood.

Fails in: pulmonary edema, pneumonia, ARDS, drowning

3

Adequate red blood cells

Enough hemoglobin must be present to carry the oxygen.

Fails in: hemorrhage, anemia, carbon monoxide poisoning

4

Proper tissue perfusion

Blood must actually reach the tissue bed.

Fails in: every form of shock; vascular occlusion

5

Off-loading at the tissue

Oxygen must release from hemoglobin and be used by the cell.

Fails in: cyanide poisoning, severe alkalosis, hypothermia

Waste removal is the other half. The same circulation that delivers oxygen carries away the waste of metabolism. Carbon dioxide leaves during gas exchange at the alveoli, other wastes drain into the lymphatic system, and the kidneys cleanse the blood and excrete waste as urine. Stop the flow and the cell both starves and drowns in its own byproducts.

The Metabolic Consequence of Shock

When perfusion fails, the cell switches to a backup that cannot keep up

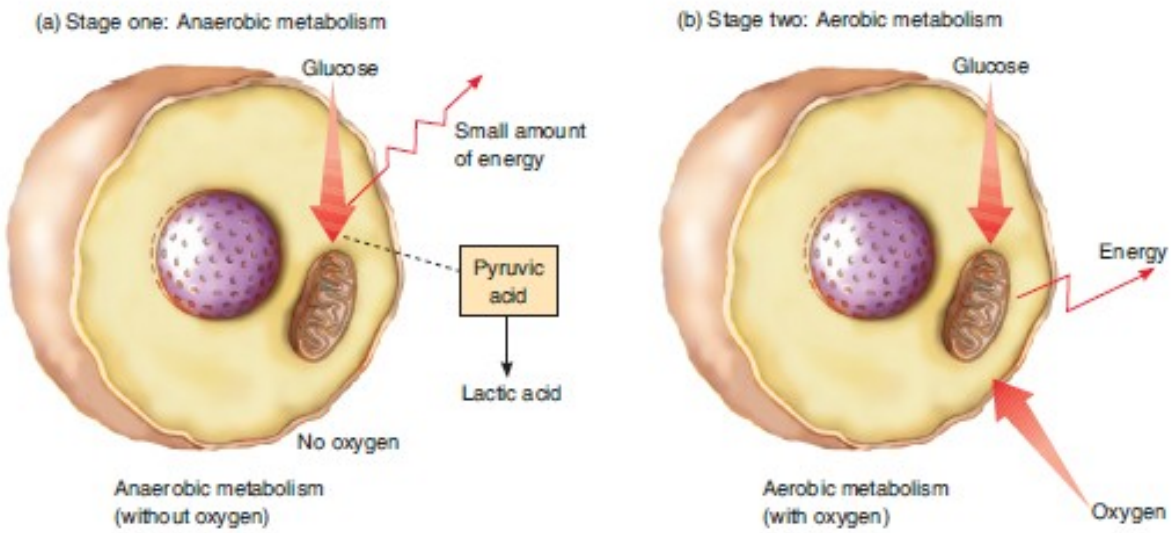

Figure 19-86 Glucose breakdown — anaerobic and aerobic

The energy collapse

Without oxygen, glucose breakdown stops after glycolysis. Cellular ATP stores are consumed far faster than they can be replaced. The sodium–potassium pump fails, sodium and water flood in, the cell swells, the membrane ruptures, and cell death follows.

Glucose is starved too

The same failure of delivery that starves cells of oxygen also starves them of glucose. Glucose that cannot enter cells stays in the blood — producing hyperglycemia in a patient whose cells are starving.

Then the body eats itself

Catecholamines, cortisol and growth hormone drive lipolysis and gluconeogenesis. Protein breakdown depletes serum albumin, which lowers colloid osmotic pressure, which loses more intravascular fluid — and worsens the hypotension that started it.

Pathogenesis of Shock

Two failures — impaired glucose use and impaired oxygen use — feeding one downward spiral

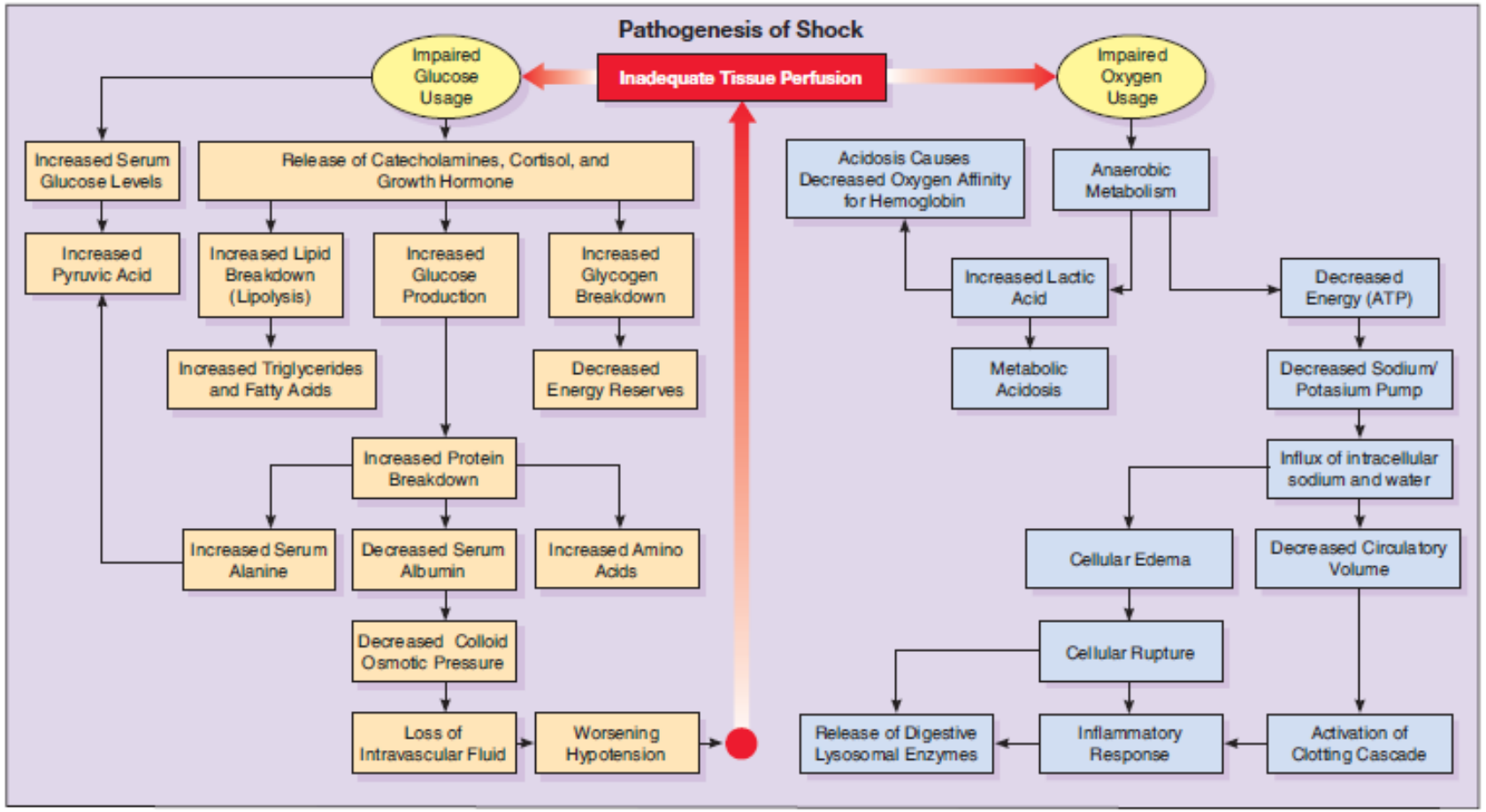

Figure 19-87 Pathogenesis of shock in the human

Compensation, Decompensation, Irreversibility

Three stages — and only the first two are reliably survivable

1 Compensated

Falling cardiac output is detected by baroreceptors as a drop in arterial pressure. The sympathetic nervous system and the renin–angiotensin system activate to restore pressure.

Signs: tachycardia, tachypnea, anxiety or restlessness, cool and pale skin, delayed capillary refill, narrowing pulse pressure. Blood pressure is still NORMAL.

2 Decompensated

The cause is too severe or progressing too fast; compensatory mechanisms can no longer keep up.

Signs: falling blood pressure, altered mental status, weak and thready or absent peripheral pulses, marked tachycardia that may begin to slow, decreased urine output, dysrhythmias.

3 Irreversible

The shock state has progressed to a point where correction is no longer possible, even if perfusion is restored. Cell and organ damage is too extensive.

The patient may transiently respond to resuscitation and still die hours or days later of organ failure.

The whole point of prehospital shock care

Recognize the patient in stage one. Early intervention can reverse many of the signs of shock. By the time blood pressure falls, compensatory reserve is largely spent — and in children and healthy young adults, that fall happens suddenly and late. Waiting for hypotension to confirm your suspicion is waiting too long.

Types of Shock

Classified by cause — but every one ends at the same cellular endpoint

Type	Failing component	Common causes	Distinguishing features
Cardiogenic	Pump	Severe left ventricular failure, acute MI, congestive heart failure, sustained dysrhythmia	Pulmonary edema, altered mentation, oliguria; fluid may worsen it
Hypovolemic	Fluid	Internal or external hemorrhage, long bone and open fractures, severe dehydration, plasma loss from burns, excessive sweating, DKA	The "classic" picture: pale cool skin, tachycardia, narrowing then falling pressure
Neurogenic	Container	Brain or spinal cord injury causing autonomic imbalance and massive vasodilation	Warm, dry, often flushed skin below the injury; relative bradycardia rather than tachycardia
Anaphylactic	Container	Repeat exposure to an antigen; massive mediator release	Very rapid onset; urticaria, angioedema, bronchospasm, GI symptoms
Septic	Container (and pump)	Infection entering the bloodstream; systemic inflammatory response	Fever or hypothermia, warm skin early, progresses to multiple organ dysfunction
Obstructive*	Pump (mechanically blocked)	Tension pneumothorax, cardiac tamponade, massive pulmonary embolism	JVD with clear or unequal lung sounds; often immediately correctable

**Obstructive shock is not in the chapter's original five categories but appears in current EMS education standards and certification exams.*

Pathogenesis of Hypovolemic Shock

How the body defends itself against volume loss — until it cannot

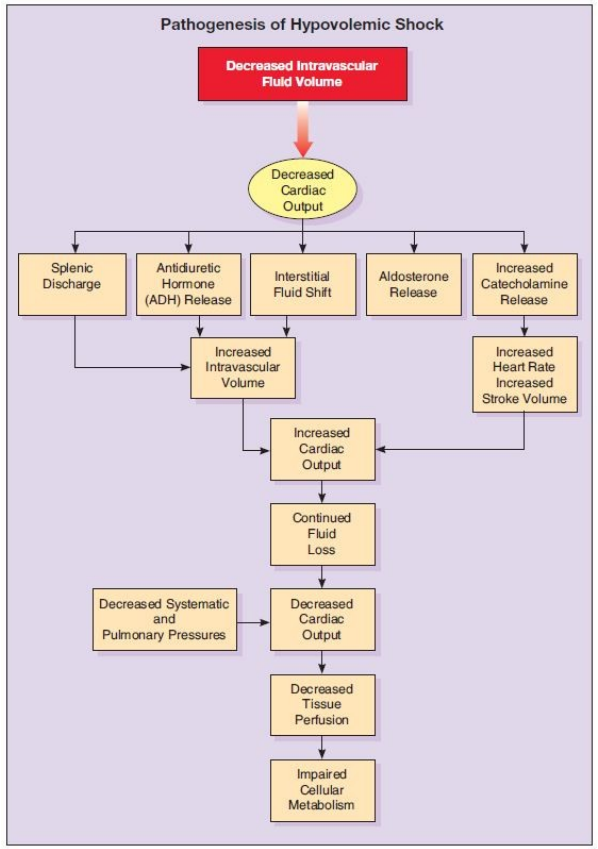

Figure 19-89 Pathogenesis of hypovolemic shock

Trace the compensation

- Intravascular volume falls, so cardiac output falls
- The spleen discharges stored red cells
- ADH is released, retaining water
- Interstitial fluid shifts into the vascular space
- Aldosterone is released, retaining sodium and water
- Catecholamines raise heart rate and stroke volume
- Together these briefly restore cardiac output

Then follow the one box that breaks it

"Continued fluid loss." Every compensatory mechanism on this chart is finite, and none of them stops the bleeding. If the loss continues, cardiac output falls again — this time with the reserves already spent — tissue perfusion drops, and cellular metabolism is impaired.

This is why hemorrhage control comes before fluid resuscitation. We cannot out-infuse an open faucet.

Distributive Shock

Normal volume, abnormal container — relative hypovolemia

1 Neurogenic

Mechanism

Injury to the brain or spinal cord produces autonomic nervous system imbalance. Sympathetic tone below the lesion is lost, causing massive vasodilation and a fall in systemic vascular resistance.

Presentation

Warm, dry, sometimes flushed skin below the injury. Relative bradycardia. Hypotension without tachycardia.

Management

Treatment mirrors other shock: airway, oxygenation, ventilation, IV access, and — critically — maintenance of body temperature, since these patients cannot thermoregulate.

2 Anaphylactic

Mechanism

Repeat exposure to an antigen triggers massive IgE-mediated release of histamine, prostaglandins and kinins from mast cells and basophils.

Presentation

Very rapid onset. Urticaria and flushing, angioedema, laryngospasm, bronchospasm, GI cramping and vomiting, profound vasodilation and capillary leak.

Management

Treatment is pharmacologic and time-critical. Epinephrine is the intervention; death can occur before the patient reaches a hospital.

3 Septic

Mechanism

Infection enters the bloodstream. A systemic inflammatory response activates multiple cell types and mediator systems, producing endothelial damage, vascular leakage and vasodilation.

Presentation

Fever or hypothermia, warm skin early, tachycardia, tachypnea, altered mentation. Progresses to dysfunction of more than one organ system.

Management

The lungs and respiratory system are most susceptible. Early recognition, fluid, source control and antibiotics drive outcome — which is why prehospital sepsis alerts exist.

Pathogenesis of Anaphylactic Shock

One mediator release, five simultaneous emergencies

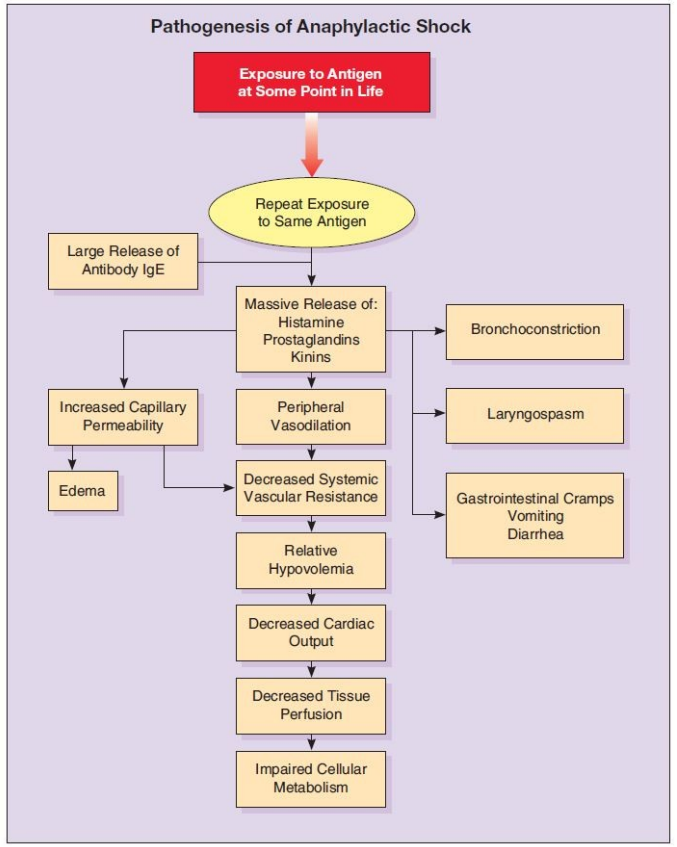

Figure 19-91 Pathogenesis of anaphylactic shock

Sensitization comes first

Note the top box: exposure to the antigen at some point in life. The first exposure does not cause anaphylaxis — it produces IgE antibodies that bind to mast cells and basophils. The patient is now sensitized and does not know it.

On re-exposure, the antigen cross-links that bound IgE, and mast cells degranulate all at once, releasing histamine, prostaglandins and kinins.

This is why a patient can eat shellfish safely for forty years and nearly die from it on a Tuesday.

Five branches, one patient

- Bronchoconstriction — wheezing, hypoxia
- Laryngospasm and laryngeal edema — stridor, the airway emergency
- GI cramping, vomiting, diarrhea
- Increased capillary permeability — edema, fluid out of the vascular space
- Peripheral vasodilation — falling SVR, relative hypovolemia, falling output

Multiple Organ Dysfunction Syndrome

Progressive impairment of two or more organ systems from an uncontrolled inflammatory response

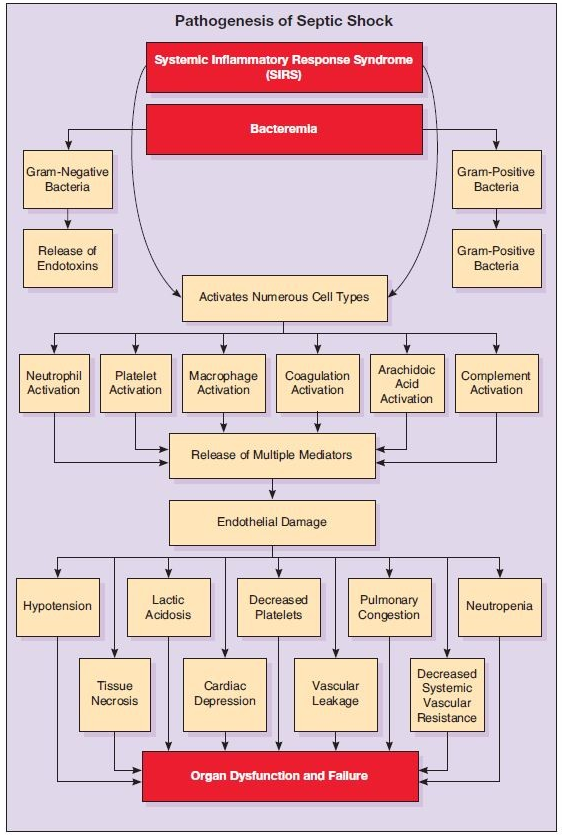

Figure 19-92 Pathogenesis of septic shock

Bledsoe, Porter & Cherry, Paramedic Care: Principles & Practice, 6th ed.

Primary vs. secondary MODS

Primary MODS: organ damage results directly from a specific cause — an episode of shock, trauma or surgery.

Secondary MODS: cells primed by the first insult are activated by a later one, producing an exaggerated inflammatory response out of proportion to the second injury.

A self-perpetuating cycle

Inflammatory mediators, toxins and plasma protein cascades produce a massive immune, inflammatory and coagulation response. The inflammatory response — which exists to protect — becomes the injury itself and enters a self-perpetuating loop.

Clinical reality

MODS does not occur in one intense crisis — it develops over a period of two, three or more weeks. Dysfunction may appear in the pulmonary, gastrointestinal, hepatic, renal, cardiovascular, hematologic and immune systems, along with decreased cardiac function and myocardial depression. Sepsis and septic shock are the most common causes, but any severe illness or injury that triggers a massive systemic inflammatory response can do it. There is no specific therapy: only early recognition and supportive measures.

Part 5 — Key Takeaways

1 **Shock is inadequate perfusion.**

Not a blood pressure. A patient with a normal pressure can be in shock, and usually is before the pressure ever moves.

2 **Pump, fluid, container.**

Every shock state is a failure of one or more of these three. Classify at the doorway using this model instead of a memorized list.

3 **All shock ends at the mitochondrion.**

Different causes, identical cellular endpoint: oxygen cannot be delivered or used, ATP collapses, pumps fail, cells die.

4 **Shock is a positive feedback loop.**

Hypoperfusion causes changes that worsen hypoperfusion. It does not plateau on its own, which is why it is progressive and fatal if uncorrected.

5 **Compensation is the window.**

Tachycardia, tachypnea, anxiety, cool skin, delayed capillary refill, narrowing pulse pressure. Act here, not after the pressure falls.

6 **Today's shock is next week's MODS.**

Minimizing the depth and duration of hypoperfusion is the only prevention we have for organ failure days later.

Part 6

The Body’s Defenses
Against Disease and Injury

1. Infectious agents
2. Three lines of defense
3. The immune response
4. Inflammation & healing
5. Hypersensitivity & stress

Infectious Agents

Five categories — and only some of them can be treated

1 Bacteria

Single-celled organisms — internal cytoplasm inside a rigid cell wall. Cultured and identified readily in most hospital labs; categorized by appearance after Gram staining. Some form a capsule outside the cell wall that resists digestion by phagocytes. Many release poisonous chemicals: exotoxins and endotoxins.

Treatable with antibiotics. Cause many common infections.

2 Viruses

Much smaller than bacteria — visible only by electron microscope. No organized cell structure except a protein capsid surrounding the genetic material, DNA or RNA; some add an outer envelope. Symptoms may be delayed, because the virus is hidden inside the host cell. Viruses produce no toxins yet still cause serious illness.

Cause most infections. Very difficult to treat; often nothing beyond symptomatic care.

3 Fungi

Yeasts and molds. More like plants than animals. Infections are called mycoses.

Rarely cause serious human disease outside minor skin infections — except in immunocompromised patients.

4 Parasites

Range from single-celled protozoa to large intestinal worms.

Treatment depends entirely on the organism and its location in the body.

5 Prions

Differ from viruses: smaller, made entirely of protein, and lacking a protective capsid.

Extraordinarily resistant to standard disinfection and sterilization. No effective treatment.

Antibiotics work on bacteria because bacteria are prokaryotes — they have structures our eukaryotic cells do not. That is why the same drugs are useless against viruses.

Bacterial Toxins and Sepsis

Many bacteria do their damage chemically

E Exotoxins

Proteins actively secreted and released by a living bacterial cell during growth.

Highly potent and often specific in their action. Because they are proteins, the body can raise antibodies against them and they can be neutralized — which is how tetanus and diphtheria toxoid vaccines work.

Examples: tetanus, botulism, diphtheria, some strains of staphylococcus and streptococcus.

N Endotoxins

Part of the outer cell wall of gram-negative bacteria, released largely when the organism dies and breaks apart.

They trigger the inflammatory process and produce fever. They cannot be neutralized by antitoxin the way exotoxins can.

This is the mechanism behind much of gram-negative septic shock — and part of why a patient can transiently worsen as antibiotics begin killing organisms.

Septicemia (sepsis)

The systemic spread of toxins through the bloodstream. The danger of sepsis is not primarily the organism — it is the body's own overwhelming inflammatory response to it. Mediator release produces widespread vasodilation, endothelial damage and capillary leak, direct myocardial depression, and activation of the coagulation cascade.

That combination is why septic shock is simultaneously a container problem, a fluid problem and a pump problem, and why it progresses to multiple organ dysfunction syndrome. Prehospital recognition matters enormously: time to fluid, time to antibiotics and time to source control drive survival.

Three Lines of Defense

External and nonspecific, internal and nonspecific, internal and specific

1 Anatomic barriers

External · Nonspecific

Skin, mucous membranes, tears, saliva, gastric acid, normal flora, the mucociliary escalator, coughing and sneezing.

They do not identify what they are excluding — they simply keep everything out.

2 Inflammatory response

Internal · Nonspecific

Activates within seconds to minutes of injury. Treats every insult the same way regardless of cause.

Involves multiple cell types and multiple plasma protein systems. Transient — it has no memory.

3 Immune response

Internal · Specific

Slow to develop but precisely targeted at one antigen.

Involves one cell type (lymphocytes) and one plasma protein (immunoglobulin). Long-term — it remembers.

Inflammatory vs. immune response — the five differences

	Inflammatory response	Immune response
Speed	Fast	Slow
Specificity	Nonspecific	Specific
Duration / memory	Transient — no memory	Long-term — memory
Plasma systems	Multiple (complement, coagulation, kinin)	One (immunoglobulin)
Cell types	Multiple (granulocytes, monocytes, macrophages)	One (lymphocytes)

The Immune Response

Two branches from one decision: chemical attack or physical attack

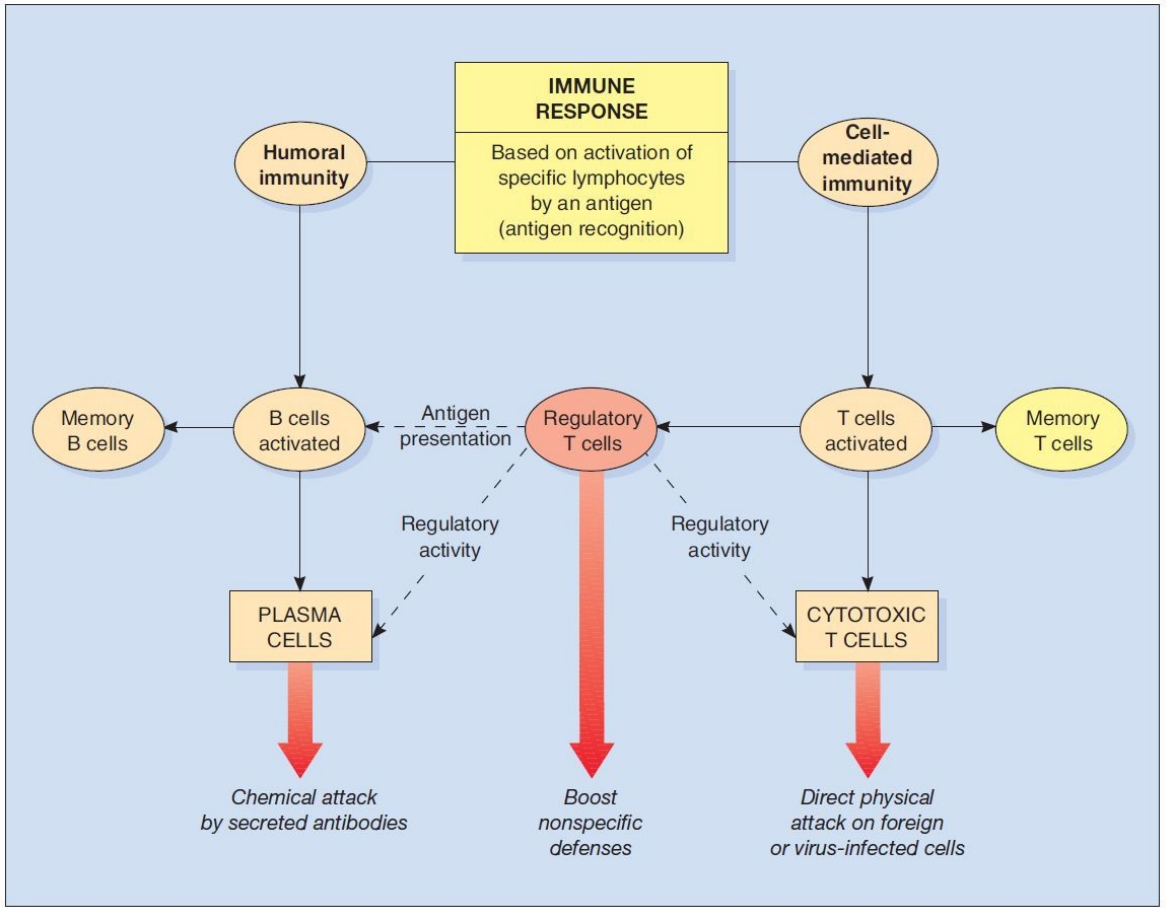

Figure 19-93 Humoral and cell-mediated immunity — an overview

How it works, in one sentence

The immune system detects antigens as foreign — "non-self" — and produces antibodies that combine with those antigens to control or destroy them.

B Humoral immunity — B cells

B lymphocytes do not attack antigens directly. Activated B cells become memory B cells and plasma cells; plasma cells secrete antibodies that mount a chemical attack. Produces long-term immunity to specific antigens.

T Cell-mediated immunity — T cells

T lymphocytes do not produce antibodies. Activated T cells become memory T cells and cytotoxic T cells, which mount a direct physical attack on foreign or virus-infected cells. Regulatory T cells coordinate both branches and boost nonspecific defenses.

Types of Immunity

Where it comes from, and how long it lasts

Natural vs. acquired

Natural immunity — inborn, part of the genetic makeup of an individual or species. Present without any prior exposure.

Acquired immunity — develops as the outcome of an immune response.

Active acquired: generated by the host's own immune system after exposure to an antigen. Long-lasting. Infection or vaccination.

Passive acquired: transferred from an outside source. Temporary. Maternal antibodies across the placenta, breast milk, immune globulin.

Primary vs. secondary response

Primary immune response — the first exposure to an antigen. Slow: it takes days to weeks to produce meaningful antibody, because the specific B and T cell lines must be selected and expanded from scratch.

Secondary (anamnestic) response — any later exposure to the same antigen. Fast and much larger, because memory cells already exist.

That difference is the entire principle behind vaccination: we generate the slow primary response deliberately, under safe conditions, so the dangerous exposure meets a secondary response.

Fetal, neonatal and aging immune function

1 In utero and newborn

Maternal antibodies cross the placenta into fetal circulation and are also passed in breast milk — passive acquired immunity protecting the child through the first months of life.

2 Childhood

As the immune system matures, the infant's own immunoglobulin levels rise while maternal antibody wanes. The overlap is why the vaccination schedule is timed as it is.

3 Older adults

Immune function deteriorates with age, with the primary assault on T cell function. After about 60, hypersensitivity responses and T cell responses to infection both decline.

Antigens, Self-Recognition and Blood Groups

How the body decides what counts as foreign

Immunogens — not every antigen triggers a response

An immunogen is an antigen that actually triggers an immune response. To do so it must have sufficient foreignness, sufficient size, sufficient complexity, and be present in sufficient amounts.

HLA and MHC: Histocompatibility locus antigens are the markers by which the body recognizes self from foreign. The major histocompatibility complex sits on chromosome 6 and determines the compatibility of grafted or transplanted tissue.

Blood group antigens

Two ABO antigens may be present on the erythrocyte surface: A and B. Type A carries only A antigens; type B only B; type AB carries both and is the universal recipient; type O carries neither and is the universal donor.

The Rh factor — Rh antigen D — is separate. Incompatibility between Rh positive and Rh negative blood can cause harmful immune responses, which is the basis of Rh isoimmunization in pregnancy.

ABO blood groups — antigens and antibodies

Blood type	Antigen present on erythrocyte	Antibody present in serum	Practical meaning
O	None	Anti-A and Anti-B	Universal donor — no antigens for a recipient to react against
A	A	Anti-B	Can receive A or O
B	B	Anti-A	Can receive B or O
AB	A and B	None	Universal recipient — no antibodies to attack donor cells

Antibodies

Y-shaped proteins that fit one antigen like a key in a lock

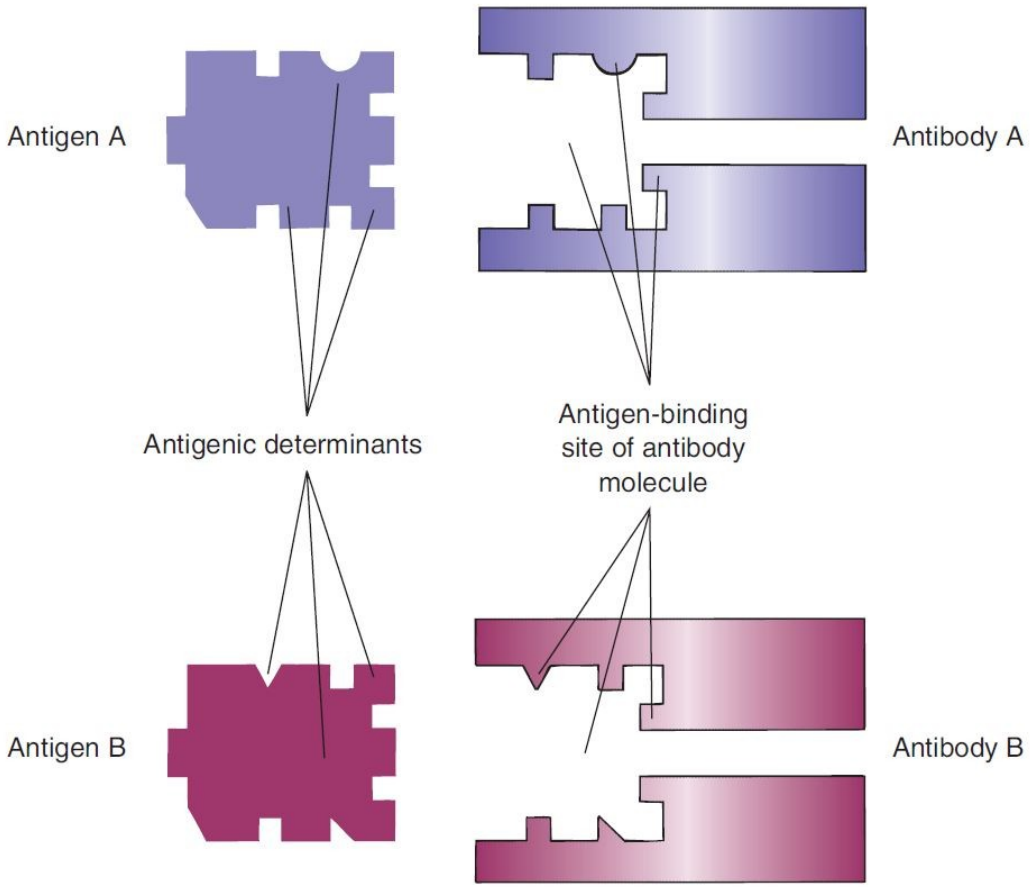

Figure 19-97 Antigen–antibody binding

Structure

All antibodies are immunoglobulins. The molecule is a Y-shaped arrangement of chains; the tips of the Y form antigen-binding sites shaped to fit one specific antigenic determinant. Change the shape of the antigen and the antibody no longer fits.

Direct effects on antigens

- Agglutination — clumping antigens together
- Precipitation — making soluble antigens fall out of solution
- Neutralization — blocking the antigen's harmful site

Indirect effects

- Enhancement of phagocytosis (opsonization) — tagging the target so phagocytes recognize it
- Activation of plasma proteins — particularly the complement system

The Five Classes of Immunoglobulin

Same basic molecule, five different jobs

IgM

The largest immunoglobulin — a pentamer. First antibody produced in a primary response.

A rising IgM suggests a current or very recent infection.

IgG

The memory antibody. Recognizes repeated invasions by an antigen. Most abundant in serum.

The only class that crosses the placenta — the source of newborn passive immunity.

IgA

Present in mucous membranes and secretions — tears, saliva, respiratory and GI mucus, breast milk.

The antibody of the secretory (mucosal) immune system, guarding the body's entry points.

IgE

The least concentrated immunoglobulin in serum — and the one that matters most in EMS.

Binds to mast cells and basophils. IgE-mediated degranulation is the mechanism of allergy and anaphylaxis.

IgD

Present in very low concentrations. Function is largely as a B cell surface receptor.

Little direct clinical relevance in prehospital care.

The one to know cold: IgE. It is present in the smallest amount of any immunoglobulin and is responsible for the most time-critical medical emergency an EMS provider treats. Sensitization means IgE specific to an allergen is now sitting on the surface of the patient's mast cells, waiting.

Cell-Mediated Immunity

T cells do not make antibodies — they attack directly

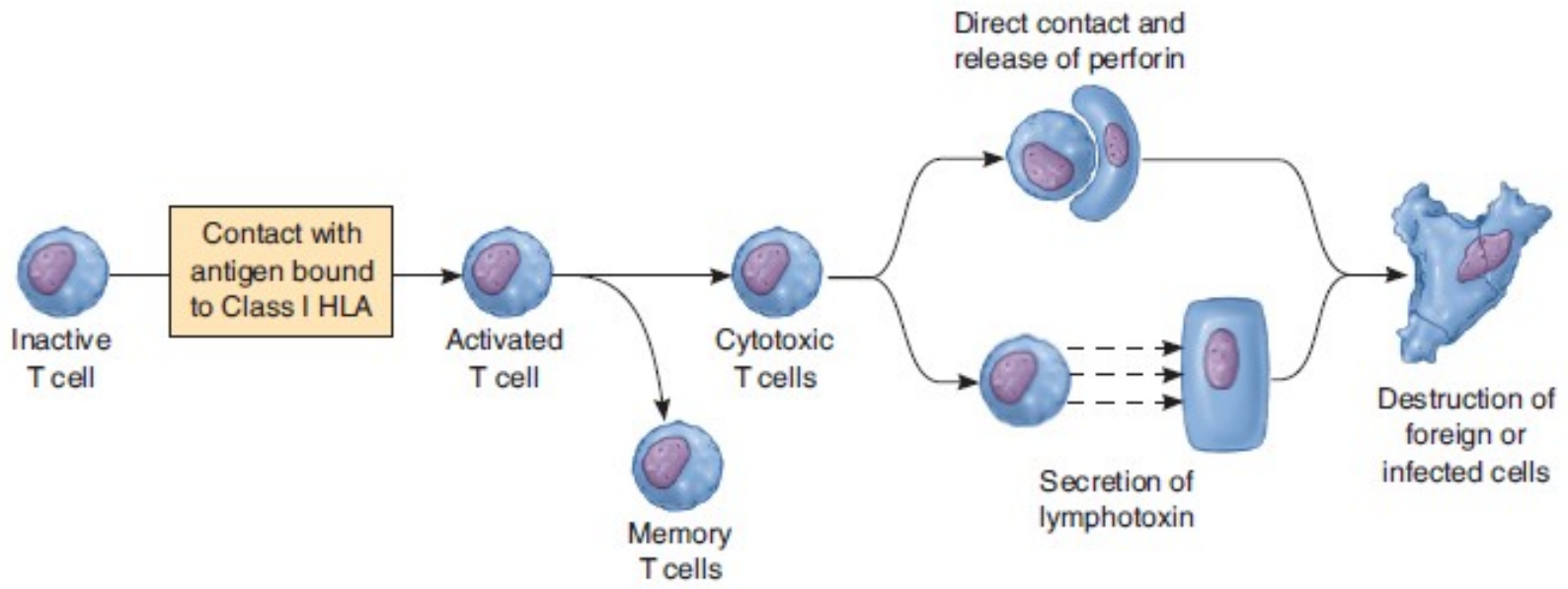

Figure 19-98 Physiology of cytotoxic T cells

Memory cells

Enable the rapid secondary response on later exposure

T_e cytotoxic (Tc)

Kill infected or foreign cells directly — perforin and lymphotoxin

Helper (T_H)

Coordinate the response; activate B cells and cytotoxic T cells

Suppressor (T_S)

Shut the response down when it is no longer needed

Delayed hypersensitivity (T_D)

Transfer delayed hypersensitivity reactions

Inducing the Immune Response

Before any antibody exists, three processes must occur — and three cells must talk to each other

The induction sequence — three processes, in this order

1 Antigen processing

A macrophage or other antigen-presenting cell ingests the antigen and breaks it into fragments.

2 Antigen presentation

The fragment is displayed on the cell surface, bound to an HLA molecule that marks it as non-self.

3 Antigen recognition

A helper T cell reads the displayed fragment and commits the system to a response.

4 Control

Other parameters shut the response down when it is no longer needed, so it does not destroy host tissue.

Three key cellular interactions — the helper T cell sits at the centre of all three

1 Presenting cell to TH

The antigen-presenting cell shows the processed fragment to a helper T cell. Nothing downstream happens until this handshake succeeds.

This is the step that distinguishes self from non-self. Get it wrong in one direction and infection wins; wrong in the other and you have autoimmunity.

2 TH to B cell

The activated helper T cell licenses the B cell to divide and differentiate into plasma cells and memory B cells.

Plasma cells secrete antibody — the humoral arm. Memory cells are why the secondary response is faster and larger than the primary.

3 TH to cytotoxic T

The helper T cell also activates cytotoxic T cells, which kill infected and foreign cells directly using perforin and lymphotoxin.

This is the cell-mediated arm. No antibody is involved at any point.

4 Where it breaks

Both arms depend on one cell. HIV infects and destroys helper T cells, which is why a single cell line's loss collapses humoral and cell-mediated immunity together.

Corticosteroids, transplant anti-rejection drugs and biologics suppress these same interactions deliberately.

Inflammation

The body's response to cellular injury — fast, nonspecific and temporary

Four functions of inflammation

1 Destroy and remove

Eliminate unwanted substances — organisms, dead tissue, foreign material.

2 Wall off

Contain the infected and inflamed area so it cannot spread.

3 Stimulate

Trigger and support the specific immune response.

4 Promote healing

Set up the repair process that follows.

Four phases

1 Acute inflammation

Triggered by any injury to the body's cells, lethal or not. Blood vessels contract then dilate, vascular permeability increases, and white cells and plasma proteins arrive to destroy the invader and begin healing.

2 Chronic inflammation

Inflammation lasting longer than two weeks. Caused by a foreign object or substance persisting in the wound, a persistent bacterial infection, or prolonged chemical irritation.

3 Granuloma formation

Large numbers of neutrophils degranulate and die, infiltrating tissue and sometimes forming a cavity of dead cells, dead tissue and fluid — pus. A granuloma walls off infection the body cannot eliminate.

4 Healing

Tissue repair and scar formation — the final stage.

The Acute Inflammatory Response

One injury, three triggers, five visible results

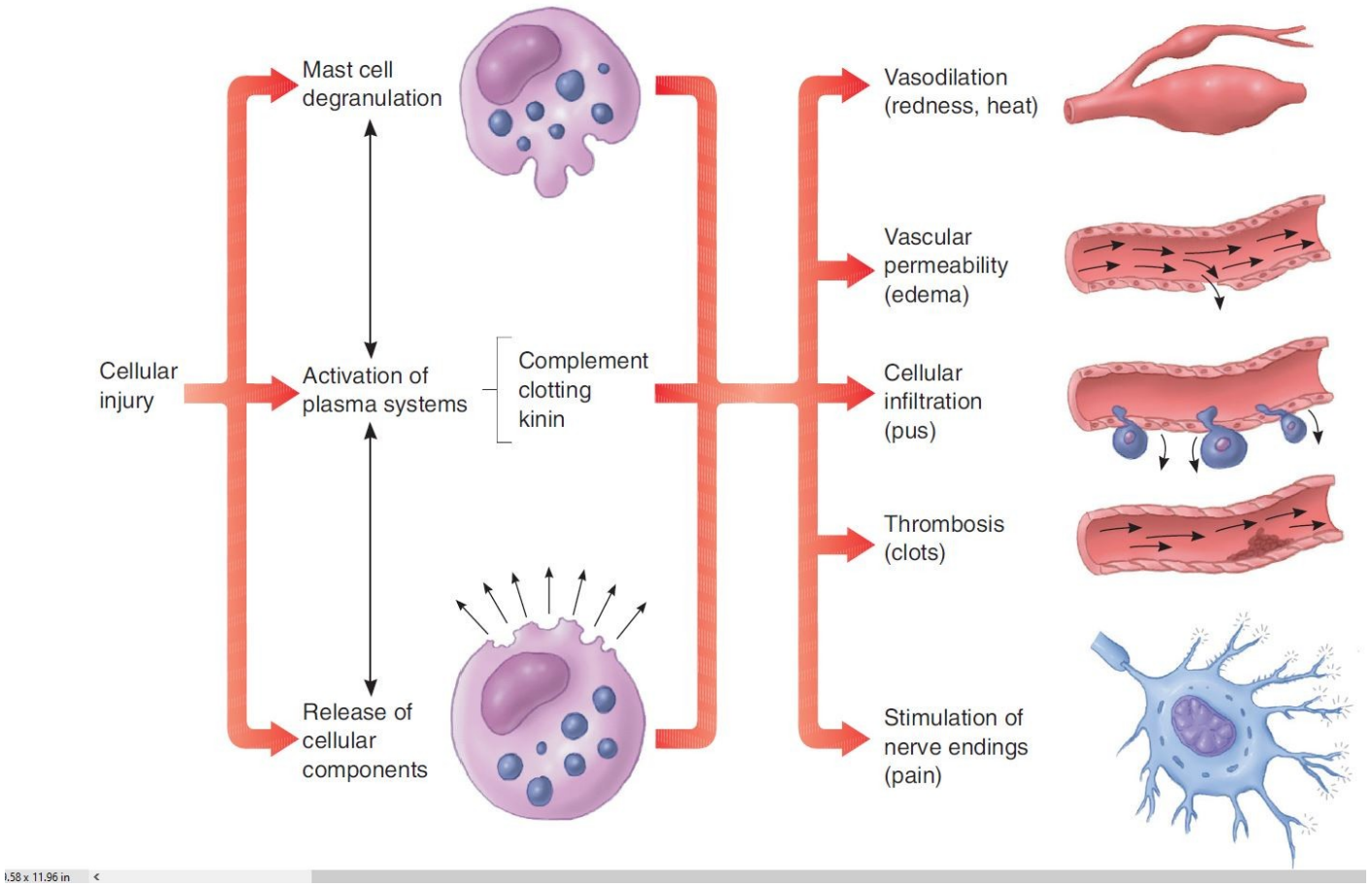

Figure 19-101 Acute inflammatory response

Three triggers

- Mast cell degranulation
- Activation of the plasma protein systems — complement, clotting and kinin
- Release of cellular components from injured cells

Five results — and the sign each produces

Vasodilation → *redness and heat*

Vascular permeability → *edema*

Cellular infiltration → *pus*

Thrombosis → *clots*

Stimulation of nerve endings → *pain*

Mast Cell Degranulation and Synthesis

The single most important figure in this section for prehospital practice

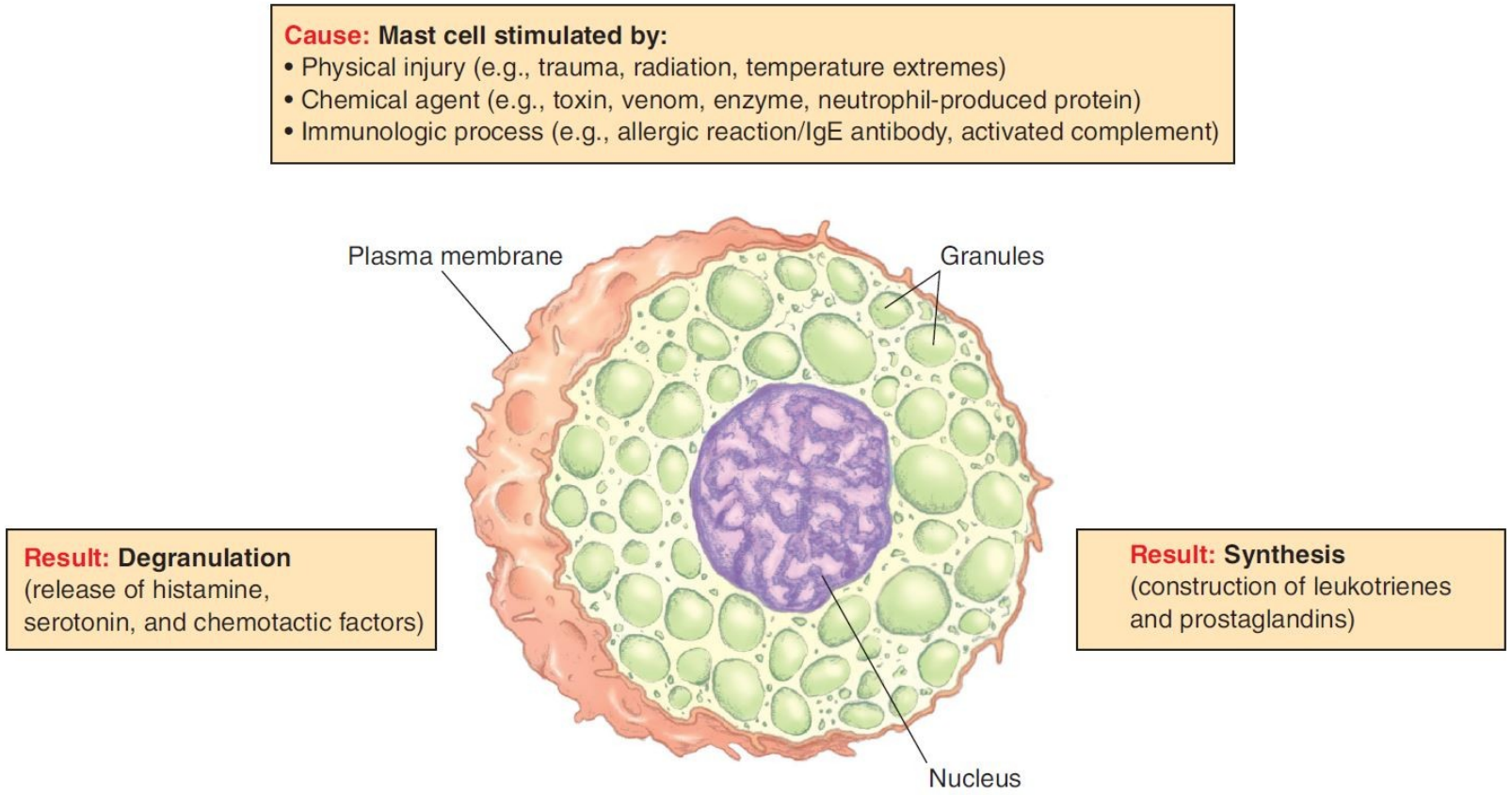

Figure 19-102 Mast cell degranulation and synthesis

The Plasma Protein Systems

Three cascades that amplify and coordinate inflammation

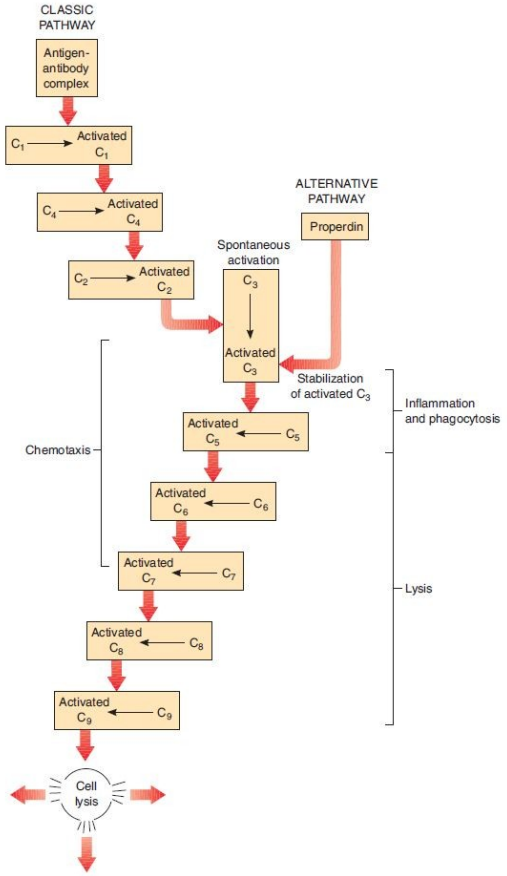

Figure 19-103 Complement cascade

Bledsoe, Porter & Cherry, Paramedic Care: Principles & Practice, 6th ed. © Pearson Education, Inc.

1 Complement system

A cascade: the first action triggers the next, and so on, amplifying at each step. Complement proteins lie inactive in blood until activated, then take part in almost every event of the inflammatory response — chemotaxis, opsonization, and finally cell lysis.

Classic pathway: activated at C1 by an antigen–antibody complex. Alternative pathway: activated at C3 without any antibody, and much faster — part of the first line of inflammatory defense.

2 Coagulation system

Forms a fibrin network at the site of inflammation. The network stops the spread of infectious agents and the products of inflammation, and forms the clot that stops bleeding.

Extrinsic pathway: triggered by injury to the vessel wall or surrounding tissue. Intrinsic pathway: triggered by exposure to elements within the blood itself. Both converge on fibrin.

3 Kinin system

Chief product is bradykinin: vasodilation, extravascular smooth muscle contraction, increased permeability, chemotaxis — and pain. The plasma kinin cascade is triggered by factors associated with the coagulation cascade.

Cellular Components of Inflammation

The cells that show up, and the chemical messages that call them

The white cells of inflammation

Cytokines — the messengers

Cytokines are proteins produced by white blood cells that act as the messengers of the immune and inflammatory responses.

Lymphokines are cytokines released by lymphocytes; they stimulate monocytes to develop into macrophages — a critical phase of the inflammatory response. Monokines are cytokines released by macrophages and monocytes.

Interleukins are an important group of cytokines; interleukin-1 is a lymphocyte-stimulating factor. Interferon is critical in the body's defense against viral infection.

Types of white blood cells

Cell type	Approximate share of all WBCs	Primary role
Neutrophils	55–70%	First responders of inflammation; phagocytosis of bacteria
Lymphocytes (T cells and B cells)	25–30%	The specific immune response
Monocytes → macrophages	Smaller fraction	Phagocytosis, debris clearance, antigen presentation
Eosinophils and basophils	Small fractions	Parasites and allergic responses; basophils release histamine

Resolution, Repair and Healing

What happens after the inflammation is finished

1 Debridement

Phagocytosis of dead cells and debris, and dissolution of fibrin clots and scabs. The site must be cleaned before it can be rebuilt.

2 Sealing

The first step of healing is sealing the wound with a clot, which dries to a scab and provides a temporary barrier.

3 Granulation

Repair begins. New capillaries and connective tissue fill the defect from the base upward.

4 Epithelialization

Epithelial cells migrate in beneath the scab, separating it from the wound surface and providing a protective covering.

5 Contraction

Six to twelve days after injury, the wound edges begin to move inward, reducing the size of the defect.

6 Maturation

Scar tissue is remodeled over months. Blood vessels disappear, leaving an avascular scar that gradually becomes stronger.

Resolution vs. repair

Resolution is complete restoration of normal structure and function, achieved by regeneration — proliferation of the remaining cells. If resolution is not possible, repair occurs instead, and scarring is the end result.

Primary intention: minor wounds with approximated edges. Secondary intention: extensive wounds that must fill in from the base.

Dysfunctional healing

Healing can fail three ways: insufficient repair, excessive repair, or new infection. Contributing causes include diabetes, hypoxemia, nutritional deficiencies and certain drugs — particularly corticosteroids.

Positioning, exercise, surgery and medication can sometimes prevent or correct it.

When Defense Goes Wrong

Too much, aimed at the wrong target, or not enough

1 Hypersensitivity

An exaggerated and harmful immune response.

Allergy — an exaggerated response to an environmental antigen. The antigens targeted are called allergens.

Anaphylactic reactions are the life-threatening extreme.

2 Autoimmunity

A breakdown in the body's tolerance for self-antigens — the immune system attacks the body's own cells.

Graves' disease, rheumatoid arthritis, myasthenia gravis, immune thrombocytopenic purpura, systemic lupus erythematosus.

3 Isoimmunity (alloimmunity)

An immune reaction between members of the same species — against another person's antigens.

Rh and ABO isoimmunization, isoimmune neutropenia, and transplant rejection.

Four mechanisms of hypersensitivity reaction

Mechanism	How it works	Timing	Clinical examples
IgE-mediated allergen reaction	Allergen cross-links IgE on mast cells; degranulation follows	Immediate — minutes	Anaphylaxis, allergic asthma, hay fever, urticaria
Tissue-specific reaction	Antibody attacks antigens present only on certain tissues	Variable	Graves' disease, myasthenia gravis, transfusion reaction
Immune-complex-mediated	Antigen–antibody complexes form and deposit in tissue	Hours to days	Systemic lupus erythematosus, serum sickness
Cell-mediated reaction	Activated directly by T cells; no antibody involved	Delayed — hours to days	Contact dermatitis, TB skin test, transplant rejection

Clinical Indications of IgE-Mediated Responses

What anaphylaxis looks like, system by system

Skin	Flushing, itching, urticaria (hives), edema and angioedema	*Often the first sign — but up to a fifth of anaphylaxis presents without skin findings. Absence of hives does not rule it out.*
Respiratory	Difficulty breathing, laryngeal edema, laryngospasm, bronchospasm	*The airway is the most immediately lethal branch. Stridor and voice change signal upper airway involvement.*
Cardiovascular	Vasodilation and increased permeability, increased heart rate; blood pressure may rise briefly before it falls	*Distributive shock. Hypotension in a patient with a suggestive history is anaphylaxis until proven otherwise.*
Gastrointestinal	Nausea, vomiting, cramping, diarrhea	*Frequently overlooked. GI symptoms plus any other system after an exposure should raise the index of suspicion.*
Nervous system	Dizziness, headache, convulsions, tearing; anxiety and a sense of impending doom	*A patient who says they feel like something terrible is happening should be believed.*

Immune Deficiencies

When the defense system is not strong enough

C Congenital (primary)

Develops when lymphocyte development in the fetus or embryo is impaired or halted. Present from birth and genetic in origin.

Rare, but these patients are profoundly vulnerable and are usually well known to the EMS system. Five named conditions follow on the next slide.

A Acquired (secondary)

Develops after birth and does not result from genetic factors. Far more common — and this is the group EMS actually transports.

Causes include nutritional deficiencies, iatrogenic causes (drugs and treatment), trauma, stress, and HIV infection progressing to AIDS.

Who is immunocompromised in your response area

1 Iatrogenic

Chemotherapy, corticosteroids, transplant anti-rejection drugs, biologics for autoimmune disease, radiation.

2 Disease-related

HIV/AIDS, leukemia and lymphoma, diabetes, chronic kidney and liver disease, asplenia.

3 Age and physiology

Newborns and older adults are both particularly susceptible to insufficient immune and inflammatory responses.

4 Replacement therapies

Gamma globulin therapy, transplantation and transfusion, and gene therapy where available.

In an immunocompromised patient, the classic signs of infection are the inflammatory response — which is exactly what they cannot mount. Assume worse than it looks.

Congenital Immune Deficiencies

Five named primary deficiencies — each one identifies which part of the system is missing

1

DiGeorge syndrome

A lack or partial lack of thymus development, producing a severe decrease in T cell production and function.

Cell-mediated immunity fails. Frequently accompanied by cardiac and facial anomalies and by hypocalcemia.

2

Bare lymphocyte syndrome

Lymphocytes and macrophages cannot produce Class I or Class II HLA antigens, so antigen presentation never works.

Severe infections that are usually fatal before age five.

3

Wiskott-Aldrich syndrome

IgM antibody production is reduced, leaving a poor response to encapsulated organisms.

Also produces thrombocytopenia and eczema. Bleeding risk on top of infection risk.

4

Selective IgA deficiency

IgA, the antibody of secretions at mucosal surfaces, is absent or markedly low. The most common of these.

Recurrent sinus, lung and gastrointestinal infections — and a risk of anaphylactic transfusion reactions.

5

Chronic mucocutaneous candidiasis

T lymphocytes are unable to mount a response specifically against Candida infections.

Persistent fungal infection of the skin, nails and mucous membranes; other immunity is intact.

These are rare — but the reasoning is not. Each deficiency names a missing component, and the missing component predicts the infection. A patient with any of these presenting with fever is a potential emergency: treat it the way you treat neutropenic fever.

Stress and Disease

The nervous, endocrine and immune systems are one interacting network

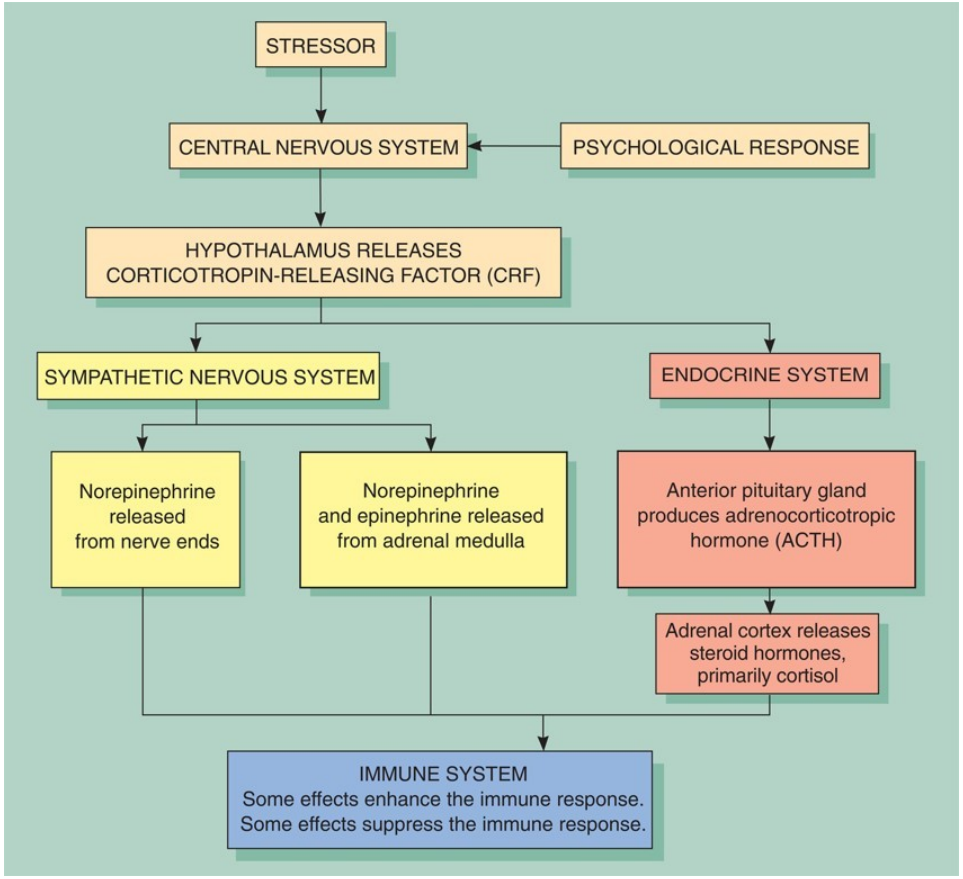

Figure 19-105 Stress response

General adaptation syndrome (GAS)

The hormones of stress

Catecholamines (epinephrine and norepinephrine), cortisol, beta endorphins, growth hormone and prolactin. Catecholamines increase heart rate, contractility, ventilation and glucose production while shunting blood away from skin and gut. Cortisol raises blood glucose, suppresses inflammation and immunity, and delays healing.

Why this closes the chapter

The interactions of psychological, neurologic, endocrine and immunologic factors that alter the immune response are called psychoneuroimmunologic regulation. Homeostasis is now described as a dynamic steady state rather than a fixed set point. Chronic stress suppresses immunity through cortisol and is associated with cardiovascular, GI, respiratory, endocrine and psychiatric disease.

Part 6 — Key Takeaways

1

Three lines of defense.

Anatomic barriers, the inflammatory response, the immune response. External and nonspecific, internal and nonspecific, internal and specific.

2

Fast and dumb, or slow and smart.

Inflammation is immediate, nonspecific and has no memory. Immunity is slow, precisely targeted, and remembers — which is what vaccines exploit.

3

B cells make antibodies; T cells attack.

Humoral immunity fights chemically at a distance. Cell-mediated immunity kills infected cells directly — the only way to reach a virus already inside a cell.

4

Mast cells are the EMS story.

IgE-triggered degranulation releases histamine immediately and leukotrienes later. That two-wave mechanism is anaphylaxis, and it is why epinephrine — not an antihistamine — is the drug.

5

Inflammation is protective until it is not.

The same process that heals a laceration produces sepsis and MODS when it runs systemically and cannot be shut off.

6

Missing signs are not reassuring.

In the immunocompromised, the very young and the old, fever and localized signs may be absent. The findings you look for are the response they cannot mount.

Putting It Together

Each case needs both parts — work them in groups

A The garden party

A 47-year-old was stung by a wasp about eight minutes ago. He is anxious, hoarse, and has audible stridor. There are no hives. Heart rate 132, blood pressure 78/40, lungs with expiratory wheezes.

Why is there no rash, and does that change your diagnosis? Name the failing circulatory component. Explain — using the mast cell figure — why an antihistamine will not save him.

B The nursing home call

An 84-year-old is "not herself" per staff. She is confused, temperature 36.1℃, heart rate 108, respirations 26, blood pressure 96/58, skin warm and dry. She has an indwelling urinary catheter and finished antibiotics last week.

What is your leading concern despite the normal temperature? Which shock category is this and why is it deceptive? What has aging done to her immune response?

C The chemotherapy patient

A 59-year-old on chemotherapy for lymphoma has a temperature of 38.4℃ and mild fatigue. Vital signs are otherwise unremarkable and he says he feels "a bit run down." His last treatment was ten days ago.

Why is this a time-critical call despite an unimpressive presentation? Which line of defense has been removed, and what does that do to your physical exam findings?