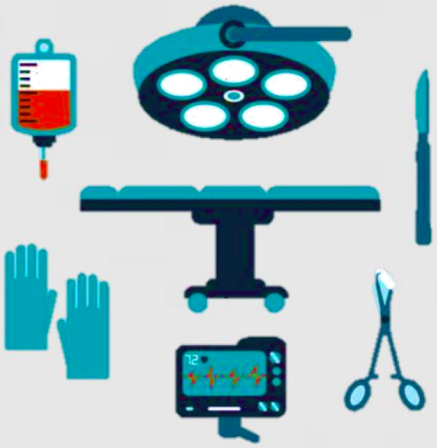

Shock and metabolic response

Objectives:

1- Explain the differences between metabolic responses to starvation and trauma.
2- Explain the effect of trauma on metabolic rate and substrate utilization.
3- Determine calorie and protein requirements during metabolic stress.
4- This session will also review macronutrients during metabolic stress, highlighting the role of conditionally-essential nutrients in specific situations.

Resources:

- Davidson's.
- 436 doctors slides.
- Surgical recall.
- 435' team work

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Color index:

Notes , Important , Extra , Davidson's

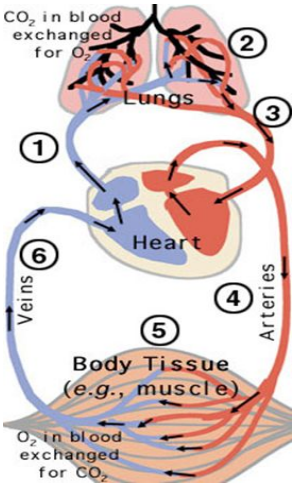
Editing file

Feedback

Shock - causes, symptoms, diagnosis, treatment, pathology 10:13 minutes *highly recommended*

Shock

What is shock?



- Inadequate oxygen delivery to meet metabolic demand.
- Results in global tissue hypoperfusion and metabolic acidosis
- Shock can occur with a normal blood pressure, and hypotension can occur without shock.

- Oxygen delivery is the function of the circulatory system.
- This system is basically*:
    - Pump (heart)
    - Pipes (vessels)
    - Solution (blood)

*Failure in any of these can result in different shock types

- Needs to function at adequate pressure, volume and carrying capacity (if you replace blood by water shock will happen because water don't have that carrying capacity)

Understanding shock:

- Inadequate systemic oxygen delivery activates **autonomic responses** (1st thing to be activated) to maintain systemic oxygen delivery:\\

Sympathetic nervous system	**Renin-angiotensin axis**
(NE, epinephrine, dopamine, and cortisol release) ✓ Causes vasoconstriction, ✓ increase in HR, and ✓ increase of cardiac contractility (cardiac output)	✓ Water and sodium conservation and vasoconstriction ✓ Increase in blood volume and blood pressure

*When body senses less O2 it tries to alarm us by sympathetic activation to make you feel anxious and to increase heart rate, sometimes this stimulation is enough and sometimes damage might happen

- Cellular responses to decreased systemic oxygen delivery
    - ATP depletion (cell can't make when cells don't receive enough O2) → ion pump dysfunction
    - Cellular edema
    - Hydrolysis of cellular membranes and cellular death (when cells die it releases mediators and tissue factors and get activation of coagulation, platelets pumping and then Disseminated Intravascular Coagulation (DIC))
- The body tries to maintain cerebral and cardiac perfusion
    - Vasoconstriction of splanchnic, musculoskeletal, and renal blood flow to shunt blood, brain and heart
- Global cellular reliance on anaerobic glycolysis and increased **lactate production**. (Aerobic glycolysis produces almost 38 ATP while anaerobic glycolysis produces 2 ATPs only)
- Systemic **metabolic lactic acidosis**

Multi-organ Dysfunction Syndrome (MODS):

Ultimately, the cells are not working, no O_2, cellular oedema, cellular death & cellular dysfunction leading to **Organ Dysfunction.**

- Progression of physiologic effects as shock ensues
  - Cardiac depression
  - Respiratory distress
  - Renal failure
  - DIC Bc the cells are dying releasing mediators and tissue factors and ultimately coagulation cascade will be activated leading to DIC.

⇒ Result is end organ failure (thus management should be done immediately. Thus we need to resus the patient before any of these happen)

Types of Shock: (Categorized based on which part of circulatory system fails)

Low Cardiac Output states	CO is normal but Low peripheral resistance states (↑ ↑ pipes)
Hypovolemic shock (↓ ↓ **solution -blood-**)	Neurogenic shock
• **bleeding** • **Dehydration** ➔ In dehydration, it's a low cardiac output state but the heart works fine. There is less blood volume to carry oxygen… as a result the mediators -as NE and hormones- will tell the heart to increase tropic volume and inotropy.the increase is up to a certain point then a shock might happen Symptoms are: tachycardia + increase SV + increase inotropy + cool temp + dry skin. The most common cause of hypovolemic hypoperfusion is hemorrhage	• **Loss of sympathetic tone** ➔ (complete loss of sympathetic tone that normally maintain some vasoconstriction) ➔ Remember: Bradycardia and vasodilation are very characteristic of the **neurogenic shock** ➔ Loss of sympathetic tone also affects the heart, so the heart cannot compensate vasodilation E.g. in spinal cord injury, sympathetic tone is lost in the same time that the vagus (parasympathetic effect) still reach the heart, leading to unopposed effect of the vagus and bradycardia. Sympathetic tone maintains some vasoconstriction.
Cardiogenic shock (↓ ↓ **pump -heart-**)	Vasogenic Shock
• **Impaired inflow** • **Primary pump dysfunction** • **Impaired outflow** ➔ In cardiogenic shock, the heart fails because of MI or HF …etc. Blood volume is ok but the heart is having a problem. We will notice blunted heart response to stimulation mediators as NE and epinephrine ➔ The patient might be tachycardic (or even bradycardic) but with echo we find that stroke volume is low… some sick hearts can increase the rate but cannot increase the volume	The heart is fine but the problem is in the vessels. A lot of … the heart need to push through all of that. Some hearts can compensate by tachycardia, but if the heart wasn't able to compensate (as in old age people) then shock might happen. • **Septic** (Bacteria-> toxins-> cell damage-> release of cell mediators thus causing uncontrolled vasodilation) • **Anaphylactic** (a lot of histamine is produced which causes vasodilation)

Shock type	Examples	HR	BP	CO	Capillary refill	Extremity temperature	SVR	Treatment
Hypovolemic	Hemorrhage Dehydration	↑	↓	↓	Delayed	Cool	High	Stop bleeding Fluid resuscitation
Cardiogenic	Myocarditis Dysrhythmia	↑	↓	↓	Delayed	Cool	High	Inotropes Caution with fluids ECMO
Distributive	Sepsis Anaphylaxis	↑	↓	↓ or ↑	Flash or delayed	Warm or cool	Low or high	Antibiotics, fluids Epinephrine
Neurogenic	Spinal cord injury Traumatic brain injury	↓	↓	↓	Flash or normal	Warm	Low	Fluid resuscitation Vasopressors
Obstructive	Tamponade Tension pneumothorax	↑	↓	↓	Delayed	Cool	High	Pericardiocentesis Chest tube
Dissociative	Carbon monoxide Cyanide	↑	Normal or ↑	↑	Normal	Normal	Low to normal	Antidotes Hyperbaric therapy

HR, heart rate; BP, blood pressure; CO, cardiac output; SVR, systemic vascular resistance.

Previous Table's Notes:

You have to know how to diagnose the shock based on hemodynamic parameters

- As long as the cardiac output is low, the body will prioritize the brain and kidney (important organs) … it will shunt the blood to brain and kidney which cases decrease in temperature, dry skin, and delayed capillary refill
- in **disruptive shock (also called vasogenic shock -including sepsis and shock)** cardiac output may increase or decrease. It decreases in cases when the heart is fatigued of too much stimulation or when the heart itself is a part of the problem. E.g. if the heart is the source of infection that caused sepsis. when the heart is fatigued of too much stimulation
- **In neurogenic shock** if the pt is tachycardic it doesn't indicate neuro shock because the sympathetic nerves are not reaching both the heart and the vessels.
- In **dissociative shock,** everything is fine except hemoglobin

Classes of Hypovolemic Shock:

What this schedule is trying to say:

- Four classes depending on blood loss
- The the more blood loss the more symptoms
- We shouldn't rely on reading patient's blood pressure because hypotension is a late finding

The doctor says he usually don't ask about classes of shock and he believes this schedule is not correct but we might get a question… also in International exams as USMLE they do ask about this

	I	II	III	IV
Blood loss (mL)	Up to 750	750–1500	1500–2000	> 2000
Blood loss (% blood volume)	Up to 15	15–30	30–40	> 40
Pulse rate (per minute)	< 100	100–120	120–140	> 140
Blood pressure	Normal	Normal	Decreased	Decreased
Pulse pressure (mm Hg)	Normal or increased	Decreased	Decreased	Decreased
Respiratory rate (per minute)	14–20	20–30	30–40	> 35
Urine output (mL/hour)	> 30	20–30	5–15	Negligible
Central nervous system/ mental status	Slightly anxious	Mildly anxious	Anxious, confused	Confused, lethargic

* Pulse pressure = stroke volume = inotropy

*Note that BP starts to dec in advanced classes (III, IV)

Treatment of Shock:

- **Goal**: Restore perfusion
- **Method**: Depends on type of Shock
- Reverse the cause. e.g. if someone has an infection that caused septic shock, it's not enough to restore BP… you have to treat the infection

Endpoints of Resuscitation in Shock management: (how to know if we managed shock? In short, the best indicator is vital organ perfusion)

- Normal vital signs (can be misleading) remember: normal heart rate and normal blood pressure does NOT indicate the absence of a shock **so we need to follow other markers that tell you about the organ damage and the 1st thing we check for is urine output** !
- Normal serum lactate levels
- Evidence of adequate tissue perfusion!! (esp. vital organs)
  - normal mental status
  - normal urine output (BEST marker, If a person was in shock and now the kidney filters normal amount (about 100cc/h) then I managed him well)
  - normal liver function.

  etc…

For lactate Note that:

1. Normal serum lactate does not always indicate the absence of shock, but elevated serum lactate indicates a problem that might be shock
2. When splanchnic circulation doesn't have enough perfusion so it produces lactate (because of ischaemic tissue)
3. Lactate isn't the best marker also because In some situations of shock, cells are too sick to produce anaerobic metabolism, so we won't find elevation of lactate

What Type of Shock is This?

- 68 yo M with hx of HTN and DM presents to the ER with abrupt onset of diffuse abdominal pain with radiation to his low back. The pt is hypotensive, tachycardic, afebrile, with cool but dry skin.
  ⍰ Hypovolemic shock (there is evidence of blood shunt)

- A 34F presents to the ER after dining at a restaurant where shortly after eating the first few bites of her meal, became anxious, diaphoretic, began wheezing, noted diffuse pruritic rash, nausea, and a sensation of her "throat closing off". She is currently hypotensive, tachycardic and ill appearing.
  ⍰ Anaphylactic shock
  Note that in all shock types you won't find bronchospasm unless if it was an anaphylactic shock

Metabolic Response to Injury

- Metabolism of substrates and micronutrients is altered by starvation and trauma. During periods of starvation, metabolic processes slow down to conserve energy and adapt to calorie deprivation. After trauma, the body's hormonal situation changes, increasing the demand for energy, proteins, and micronutrients. If nutritional requirements are not recognized and met during starvation or trauma, there may be a loss of body mass, body protein, and impairment or loss of body functions.

Surgery is an injury but it is a "controlled injury" because they manage to not cause the body to response to it

Mediating the Response:

1. The Acute Inflammatory Response
   - Cellular activation
   - Inflammatory mediators (TNF, IL1, etc)
   - Paracrine Vs endocrine effects
   - Tumor markers

2. The Endothelium (when activated or injured then will cause bad effects)
   - Selectins, Integrins, and ICAMs
   - Nitric Oxide (massive nitric oxide = very bad and severe vasodilation)
   - Tissue Factor (massive tissue factor release = DIC)

3. Afferent Nerve Stimulation produces catecholamines (e.g. cutting an afferent nerve may cause this stimulation) note that afferent nerves are widely spread almost everywhere
   - Sympathetic Nervous System
   - Adrenal Gland Medulla

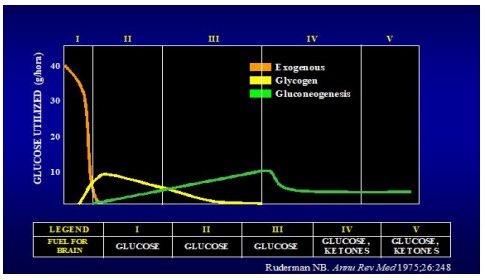
4. The Endocrine System
    - Pituitary Gland (GH, ACTH, ADP)
    - Adrenal Gland (Cortisol, Aldosterone)
    - Pancreatic (Glucagon, ↓ Insulin) (pancreas get activated because we want energy… there will be glycogenesis and glycogenolysis. But it isn't the time for insulin -not the time for anabolic hormones-, that's why every sick patient is hyperglycemic)
    - Others (Renin, Angiotensin, ↓ Sex hormones, ↓ T4)

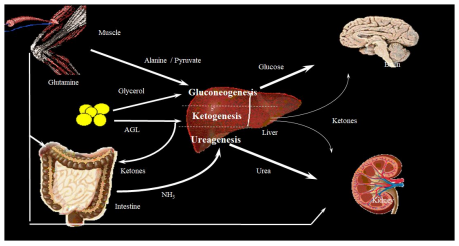
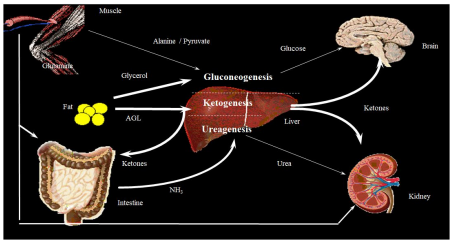
Consequences of the Response:

- Limiting injury
- Initiation of repair processes
- Mobilization of substrates (energy resources as aminoacidos from muscles, glycogen from liver, gluconeogenesis, ketones)
- Prevention of infection (more WBCs are activated by iCAM and interleukins… if too much it's harmful)
- Distant organ damage

Metabolic Response to Fasting:

- The metabolic response to fasting is an adaptation by the body to preserve protein by using alternative sources of energy.
- The carbohydrate deposits of the body last about 18 to 20 hours and new glucose is produced through gluconeogenesis of amino acids from the lean body mass
- Fasting is a part of every surgery or injury.
- Fasting includes activation of glycogenolysis, gluconeogenesis, and switching the catabolic response rapidly)



I. Starvation – Early Stage	II. Starvation – Late Stage
• The initial response to fasting is mediated by a drop in serum insulin and an increase in glucagon. During this period energy is provided mainly by glucose from gluconeogenesis. However, lipolysis generates free fatty acids which are oxidized into ketones.	• After several days, most of the body organs are using ketones (acetoacetic, propionate, and butyric acids) for energy and gluconeogenesis decreases to half of the early phase. Brain, red blood cells, and nerve tissue still rely partially on glucose for energy.
	

The aim of these two black graphs is to show that: In starvation, glucose is directed to the brain while the rest of body tissues can use ketones (when gluconeogenesis runs out and it comes to ketogenesis phase then the brain can adapt using ketones).

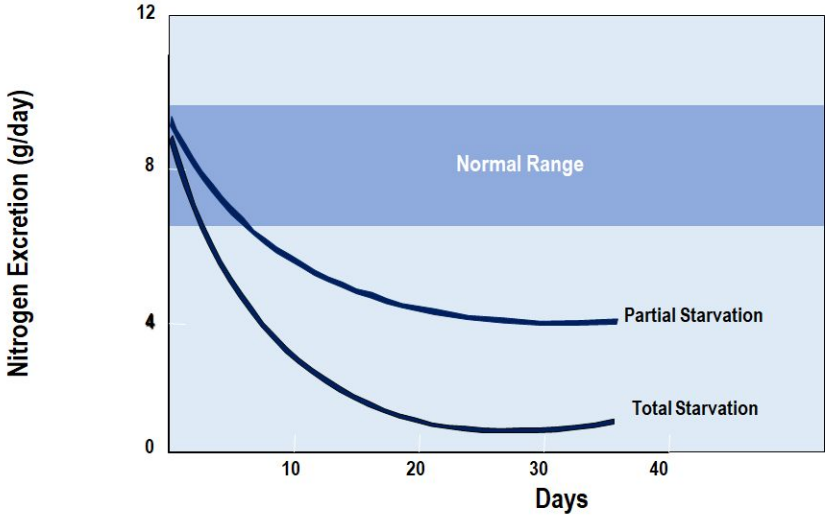
Metabolic Response to Starvation:

Hormone	Source	Change in Secretion
Norepinephrine	Sympathetic Nervous System	↓ ↓ ↓
Norepinephrine	Adrenal Gland	↑
Epinephrine	Adrenal Gland	↑
Thyroid Hormone T4	Thyroid Gland (changes to T3 peripherally)	↓ ↓ ↓

Note that in starvation NE production is less (to conserve energy). But before the person has starvation NE was elevated.

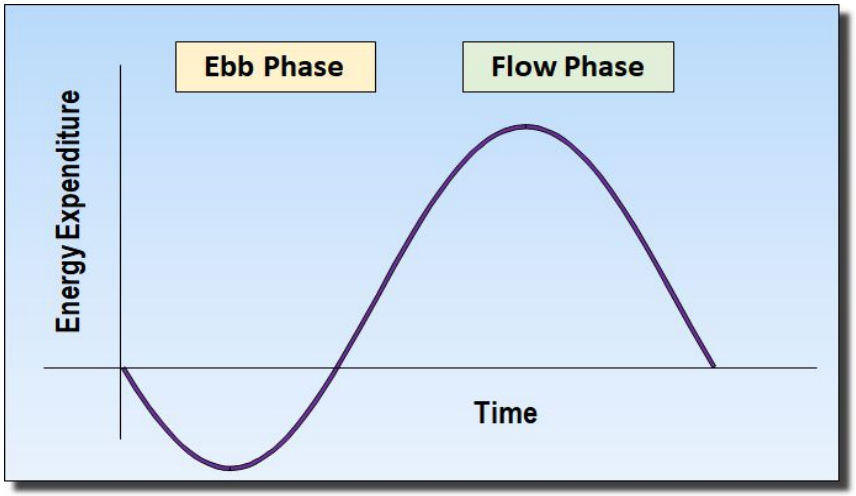
- Conservation of energy is one of the basic adaptive responses to calorie reduction; when food is in short supply, metabolic activity decreases to spare fuel.
- Adjustments in the energy requirements of the body in response to changes in caloric intake occur through the action of several hormones, primarily norepinephrine and thyroid hormone. Norepinephrine is produced by the sympathetic nervous system and the adrenal glands, located near the kidneys. Thyroid hormone T4 is produced by the thyroid gland, and is modified in the periphery to the active hormone T3. Both norepinephrine and T3 participate in the decrease in metabolic activity when calorie intake decreases.

Energy Expenditure in Starvation: (In starvation the body adapts and basal metabolic rate goes down… that's why aggressive diets won't work… you will lose weight initially then will reach plateau because the body will know it's starvation state so drops metabolic rate and thus the person feels weak in aggressive diets)



- The two lines on this graph show another adaptive response to severely reduced calorie intake.
- Urinary nitrogen excretion gradually decreases, indicating conservation of body protein and demonstrating adaptation to starvation.

Metabolic Response to Injury:

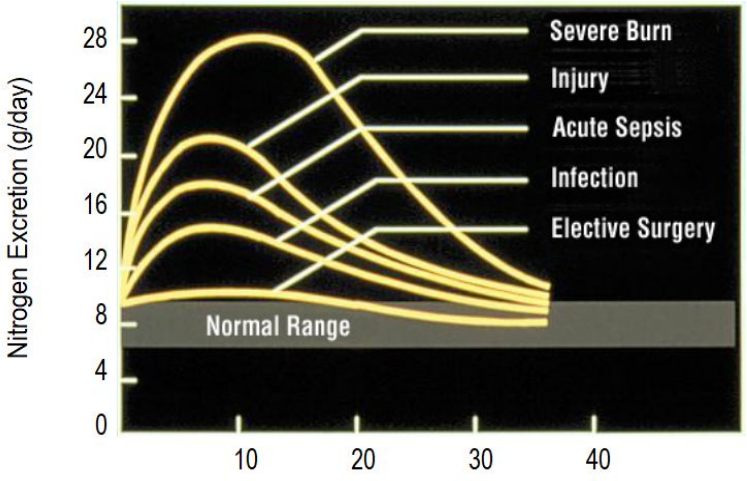


- Trauma causes major alterations in energy and protein metabolism.
- The response to trauma can be divided into the ebb phase and the flow phase. The ebb phase occurs immediately after trauma and lasts from 24-48 hours followed by the flow phase. After this, comes the anabolism phase and finally, the fatty-replacement phase.

Ebb Phase	Flow Phase
● Characterized by hypovolemic shock ● Priority is to maintain life/homeostasis ○ ↓ Cardiac output ○ ↓ Oxygen consumption ○ ↓ Blood pressure ○ ↓ Tissue perfusion ○ ↓ Body temperature ○ ↓ Metabolic rate ➔ Ebb phase conserves energy and shunts blood to important organs ➔ We need doctors to spot this phase to make an insult… because in this phase the need more protein and energy that if wasn't supplied would result in wasting	○ ↑ Catecholamines ○ ↑ Glucocorticoids ○ ↑ Glucagon ● Release of cytokines, lipid mediators ● Acute phase protein production

So Ebb phase is what makes response to injury similar to response to starvation while flow phase is what makes response to injury different from response to starvation

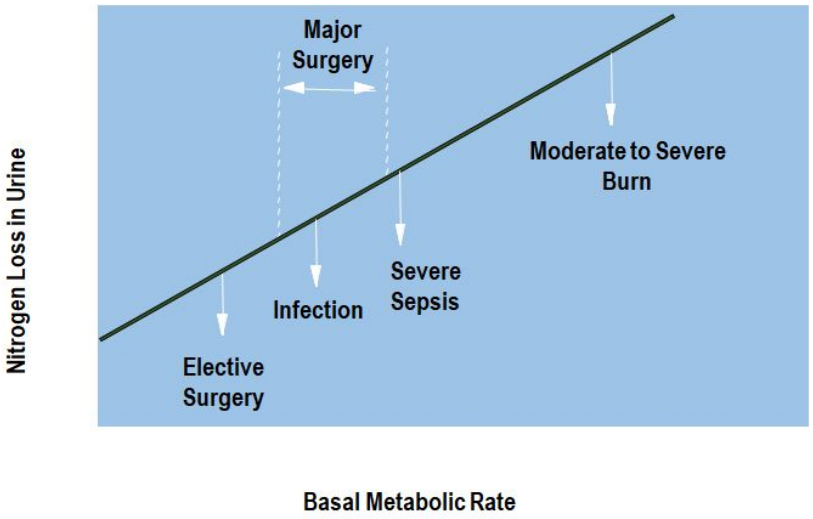
- The ebb phase is characterized by hypovolemic shock. Cardiac output, oxygen consumption and blood pressure all decrease, thereby reducing tissue perfusion. These mechanisms are usually associated with hemorrhage. Body temperature drops. The reduction in metabolic rate may be a protective mechanism during this period of hemodynamic instability.
- Endocrine response in the form of increased catecholamines, glucocorticoids and glycogen, leads to mobilization of tissue energy reserves. These calorie sources include fatty acids and glycerol from lipid reserves, glucose from hepatic glycogen (muscle glycogen can only provide glucose for the involved muscle) and gluconeogenic precursors (eg, amino acids) from muscle.



- This slide illustrates nitrogen losses in relation to trauma. With respect to protein, the greater the trauma, the greater the effect on the nitrogen balance. Similar to metabolic rate, patients experience nitrogen losses according to the severity and duration of the trauma.
- The normal range is indicated by the shaded area. The amount of protein requirement relative to calories increases in patients with metabolic stress.

One point out of this graph:
Even after benign elective surgeries - in which they try control everything as possible-, basal metabolic rate will go down and patients need support afterwards

Severity of Injury: Effects on Nitrogen Losses and Metabolic Rate



- This graph illustrates that severity of injury correlates to increasing urinary nitrogen loss and increasing energy needs. Elective surgery being least traumatic and the lowest nitrogen loss in urine, whereas burn results in an increase in basal metabolic rate and urinary loss of nitrogen.

*Moderate to severe burns are the worst
*Elective surgery is less

Comparing Starvation and Injury

	Starvation	Trauma or Disease
Metabolic rate	↓	↑ ↑
Body fuels	Conserved	Wasted
Body protein	Conserved	Wasted
Urinary nitrogen	↓	↑ ↑
Weight loss	Slow	Rapid

The body adapts to starvation, but not in the presence of critical injury or disease.

- The metabolic response to starvation can be contrasted to trauma or disease:
- Metabolic rate drops during starvation, while in trauma patients it rises in proportion to the trauma severity.
- Body fuels and body proteins are conserved during starvation, but are wasted during trauma.
- Urinary nitrogen values fall with inadequate protein and calorie intake, but increase in response to metabolic stress.
- Weight loss is slow in underfed patients but rapid in trauma patients.
- Changes in body composition with trauma usually occur two to three times faster than during starvation.

Modifying the Response how to blunt the response:

- Medication (before or after injury)
- Nutritional status
- Severity of injury that's why in surgery we try to minimize the amount of injury as possible
- Temperature (if patient is cold we try to warm him while surgery and so on)
- Anesthetic technique (relaxing the patient before incision)
- Maintaining sterility is also useful
- In ER surgery truma, you can't modify and damage will happen.

Summary: (From the slides)

- Injury (Trauma or Surgery) leads to a metabolic response
- Metabolic response to injury is an adaptive response and we can blunt some of it
- Metabolic response could overwhelm the body and lead to increased morbidity and mortality if not opposed
- We can modify the metabolic response before and sometimes after injury

Metabolism of substrates and micronutrients is altered by starvation and trauma. During periods of starvation, metabolic processes slow down to conserve energy and adapt to calorie deprivation. After trauma, the body's hormonal situation changes, increasing the demand for energy, proteins, and micronutrients. If nutritional requirements are not recognized and met during starvation or trauma, there may be a loss of body mass, body protein, and impairment or loss of body functions.

Summary:

- Shock is inadequate oxygen delivery to meet metabolic demand
- It leads to activate two systems :
    1. Sympathetic nervous system
    2. Renin-angiotensin system
- MODS characterized by
    1. Cardiac depression
    2. Respiratory distress
    3. Renal failure
    4. DIC
- Types of shock

Low Cardiac Output states	**Low peripheral resistance states (↑ ↑ pipes)**
Hypovolemic shock (↓ ↓ **solution**)	Neurogenic shock
● **bleeding** ● **Dehydration**	● **Loss of sympathetic tone**
Cardiogenic shock (↓ ↓ **pump**)	Vasogenic Shock
● **Impaired inflow** ● **Primary pump dysfunction** ● **Impaired outflow**	● **Septic** ● **Anaphylactic**

- Treatment of shock is to reverse the cause
- How do we know if our management is correct ? when we see evidence of adequate tissue perfusion esp. normal urine output
- Factors Mediating the metabolic response to injury :
    1. The acute inflammatory response
    2. The endothelium
    3. Afferent nerve stimulation
    4. The endocrine system
- Comparison of metabolic response to starvation and trauma

	Starvation	Trauma or Disease
Metabolic rate	↓	↑ ↑
Body fuels	Conserved	Wasted
Body protein	Conserved	Wasted
Urinary nitrogen	↓	↑ ↑
Weight loss	Slow	Rapid

Questions:

(cases from 434 team)

- **Case 1** : 17 years old male, diving into water.
Vital signs : BP 90/60 (low), Pulse rate :110 (High), Respiratory rate : 24 (high)
Physical examination : paralysis below C5
Cervical X-ray: C5 fracture
Hemodynamics:
Central venous pressure Decreased \ Cardiac output Decreased
Systemic vascular resistance Decreased .

The case presentation of ? ……..

-Case 2 :15 years old male, 4 day history of abdominal pain, N/V and anorexia
Vital signs: BP : 70/60 (low), Pulse rate : 130 (high), Respiratory rate 28 (high) Temperature :102.4, O2 saturation : 99%.
General examination : moderate distress from abdominal pain
Cardiac: tachycardia
Abdomen: diffuse tenderness w peritonitis
WBC : 19,600 (high), 90% segs
Hb: 14.2
Hemodynamics: Cardiac output Increased and systemic vascular resistance Decreased
Diagnosis : Perforated appendicitis.

The case presentation of ? ……..

-Case3 : 17 year old male. Training for track team.
Vital signs: BP: 70/50 (low), Pulse rate : 140 (high), Respiratory rate 35 (high)
O2 saturation : 88%
Physical examination : absent breath sounds in L lung field, distended neck veins
DX: tension pneumothorax
Hemodynamics:
Central venous pressure: Increased \ Cardiac output: Decreased \Systemic vascular resistance: Normal .

The case presentation of ? ……..

Case 4 : 3 years old male. Clothes ignited from roaster at Thanksgiving.
Vital signs: BP: 60/60 (low), Pulse rate : 170 (high), Respiratory rate : 35 (high),
O2 saturation : 89%
General examination :moderate distress
Lung:tachypneic, clear to auscultation Cardiac:tachycardic, regular
Skin:60% TBSA partial and full thickness burn
DX: 60% TBSA burn
Hemodynamics:
Cardiac output Decreased \Systemic vascular resistance Increased .

The case presentation of ? ……

Q1 : which one of the following is an evidence of adequate tissue perfusion?

a) Normal blood pressure.
b) Normal normal heart rate
c) Normal mental status
d) Normal urine output.

Q2 : which one of the following types of shock is associated with low peripheral resistance states .

a) Cardiogenic shock
b) anaphylactic shock
c) Hypovolemic shock

Q3: 15-year-old s/p trampoline injury with tetraplegia (a.k.a. "quadriplegia") with hypotension. No other injuries on CT scans. It is presentation of which type of shock?

a) Hypovolemic shock
b) Septic shock
c) neurogenic

Answers |

Case 1 : Neurogenic shock
Case 2 : Septic shock
Case 3: Cardiogenic shock
Case 4: Hypovolemic shock (LOSS OF FLUID INTO INTERSTITIUM) due to CAPILLARY LEAK.

Q1 : c and d
Q2: b
Q3: c