Kidney and Distant Organ Crosstalk in Health and Disease

By

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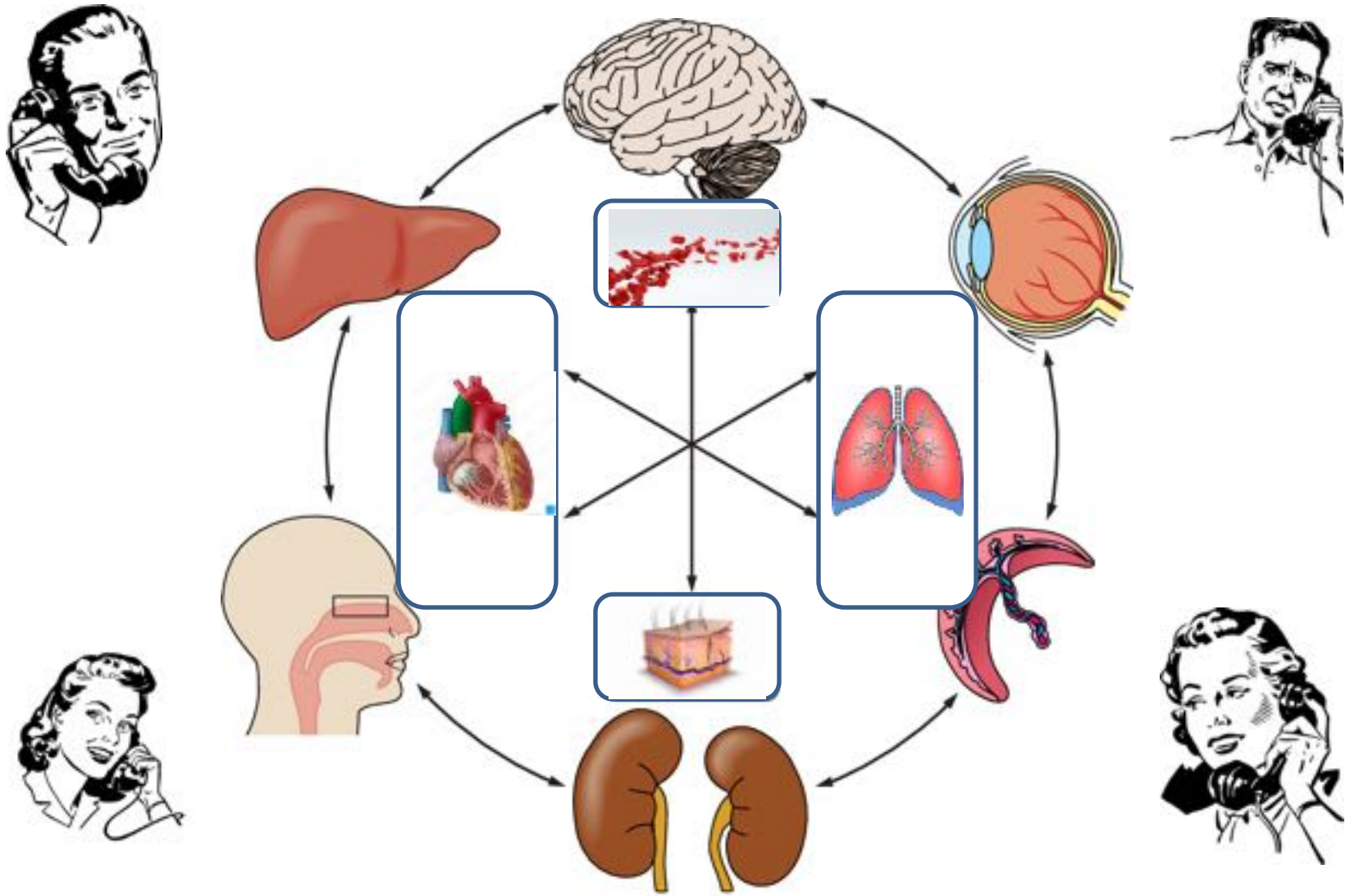
ESPNT

To respond to various metabolic demands, higher organisms have developed a system of *inter-organ communication* through which one tissue can affect metabolic pathways in a distant tissue.

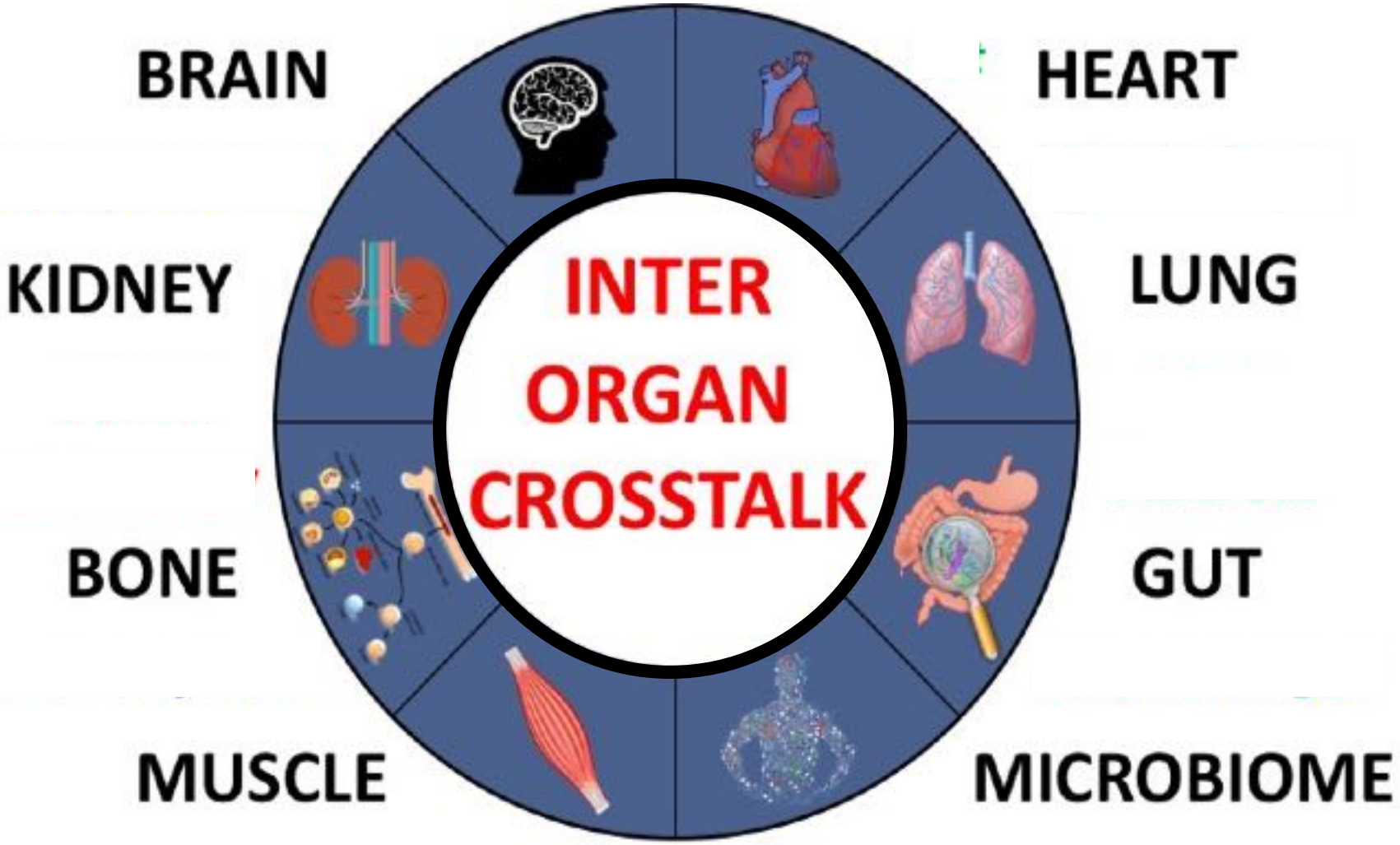
ALL systems interact with each other for our bodies to operate and survive.

Not one can survive without the others.

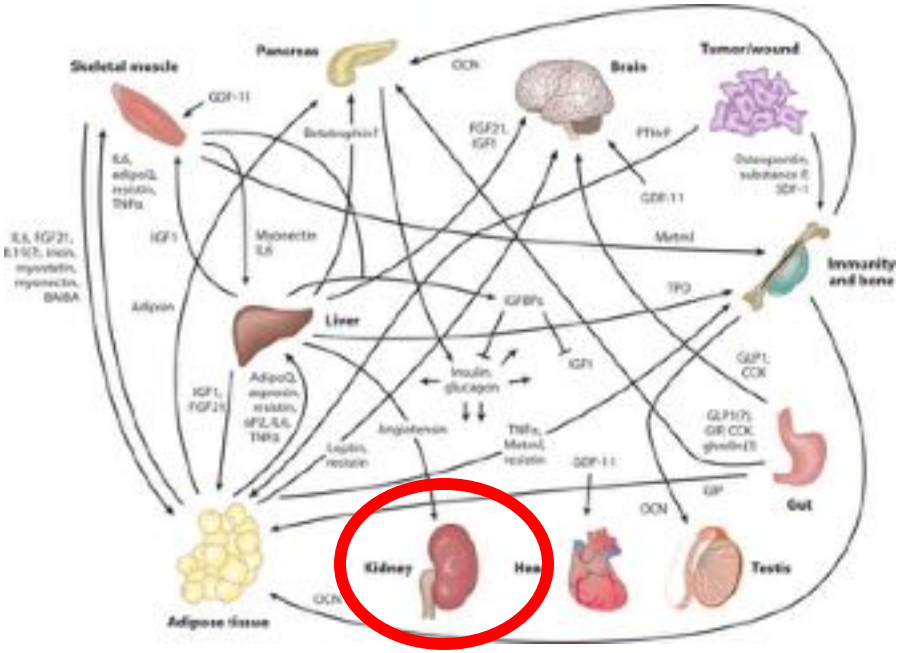


Organs "talk" to each other during normal physiology and disease.

THIS IS



Which occurs between or involves two or more organs or parts of the body.

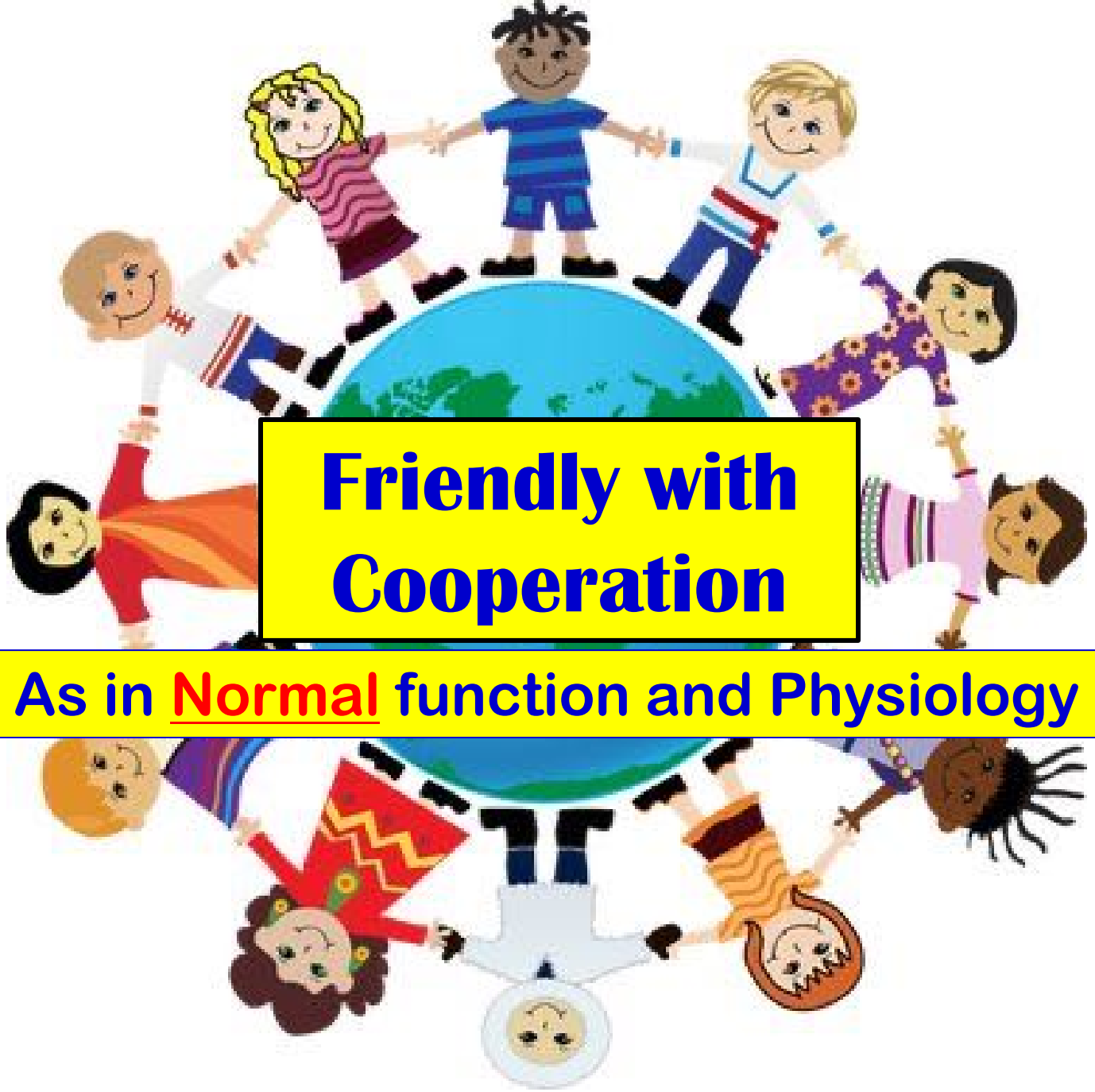


over **500** proteins of transporters, enzymes, and regulatory proteins of the *remote sensing and signaling system (RSSS)* interact with a wide range of metabolites, signaling molecules, antioxidants, nutrients, and gut microbe products to *help maintain homeostasis.*

This Organ

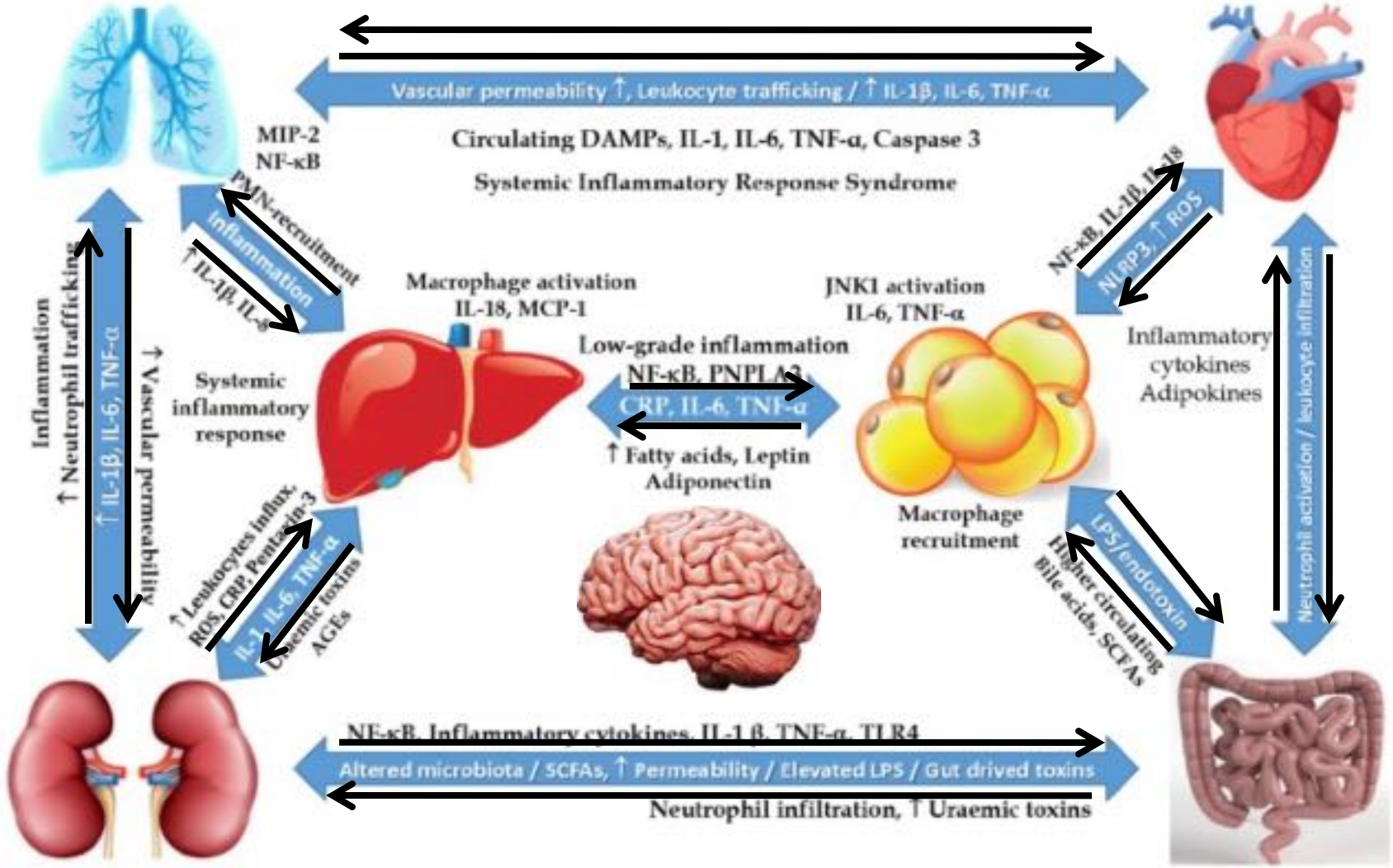
crosstalk

may be:



Friendly with Cooperation

As in Normal function and Physiology



where it is a continuum between the different systems and organs of the body.

But it may be,

Sad and sympathizing

where we observe that disease can "spread" from one organ to others.

As well, It can be,

Hostile and Offensive

With significant morbidities

It might turn to be

destructive

Either to the body own organs and tissues as in

Or to transplanted organs as in:

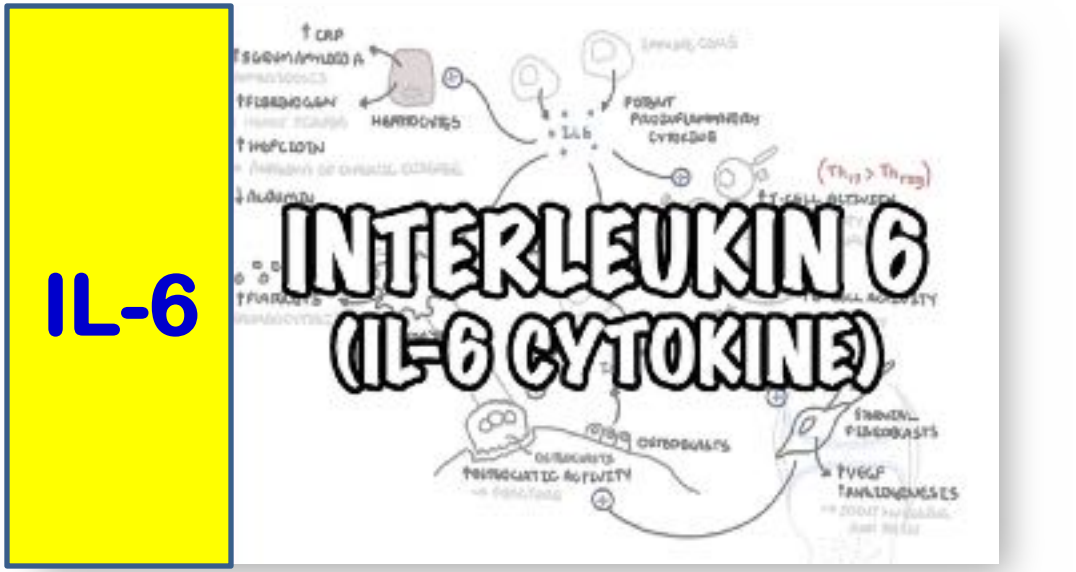
AND

It might turn to be

life-threatening


COVID-19
IL-6
COVID-19
CYTOKINE
STORM
IL-2
IL-1β
TNF-α
IL-2
IL-6
IL-1β
IL-2
IL-6

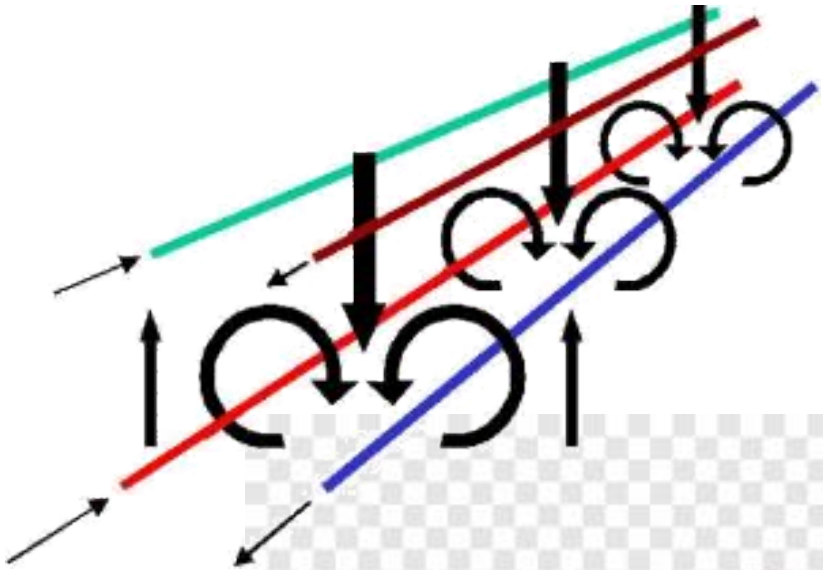
IL-6



KEY PLAYER

High IL-6 serum levels are associated with increased risk of mortality, mechanical ventilation requirements, and increased severity of SARS-CoV-2 induced pneumonia.

How do organs talk to each other ?



CROSS XTALK

MAY BE,

Wireless

Through Cytokines

Cytokines are small proteins crucial for **controlling the growth and activity of other immune system cells and blood cells**.

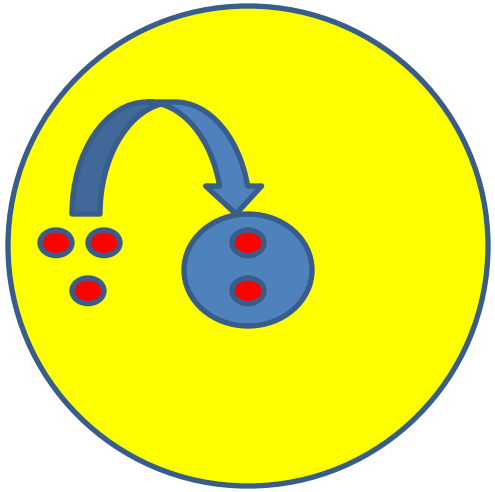
محركات الخلايا

Cytokines are produced by **a broad range of cells, including immune cells like macrophages, B lymphocytes, T lymphocytes and mast cells, as well as endothelial cells, fibroblasts, and various stromal cells**;

a given cytokine may be produced by more than one type of cell.

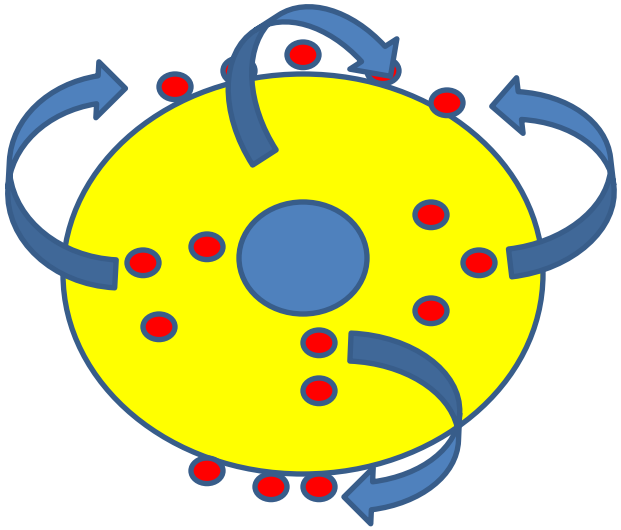
They act in different ways…

INTRACRINE



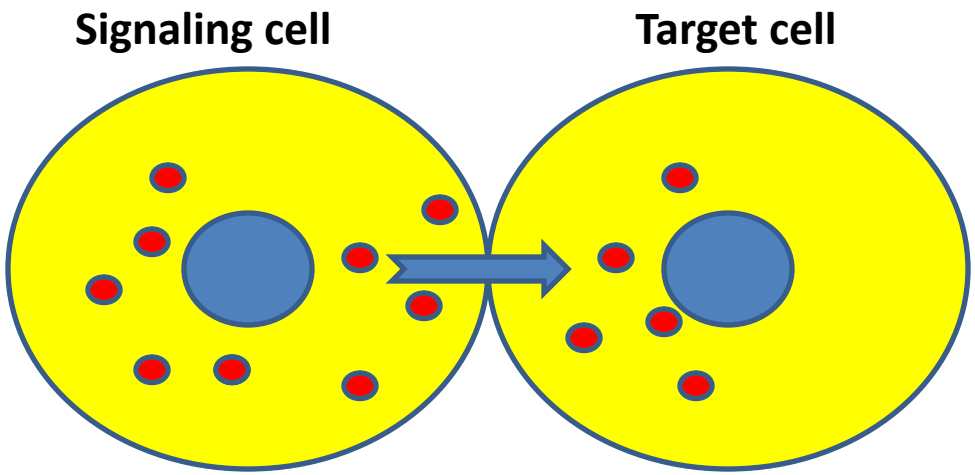
Where the cytokines act from
within the cell targeting the same cell
without moving to the intercellular space.

AUTOCRINE



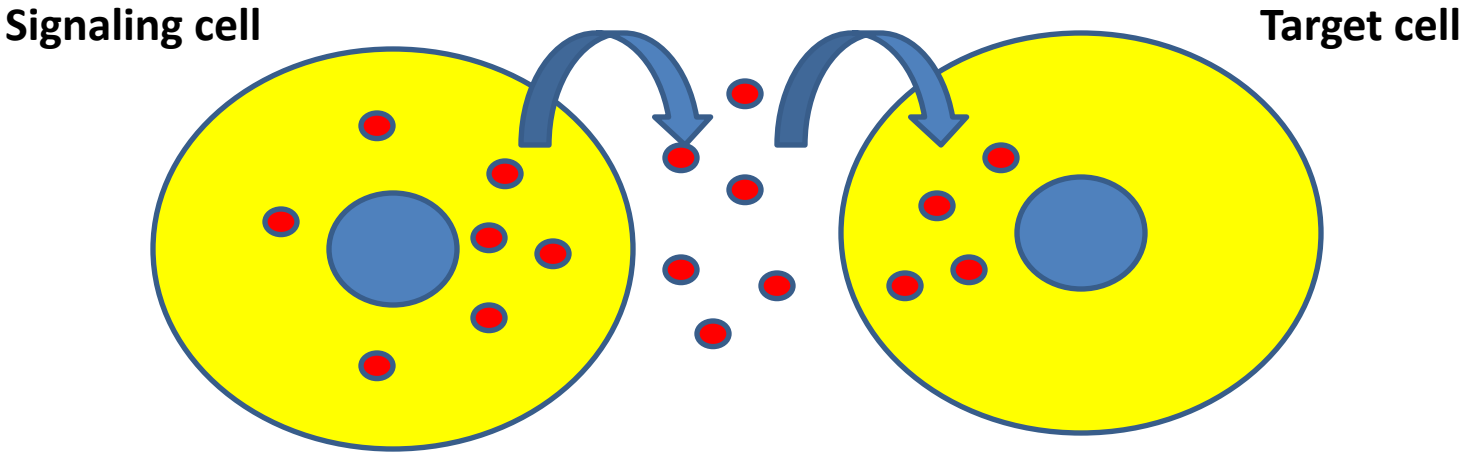
Here, the cytokines move
out of the cell to get attached to their
receptors on the outer side
of the same cell.

JUXTACRINE



The cytokines target the cells in
direct contact with the signaling cell
without appearing in the intercellular space.

PARACRINE



The cytokines
diffuse first in the extracellular space
before getting attached to the
nearby target cells.

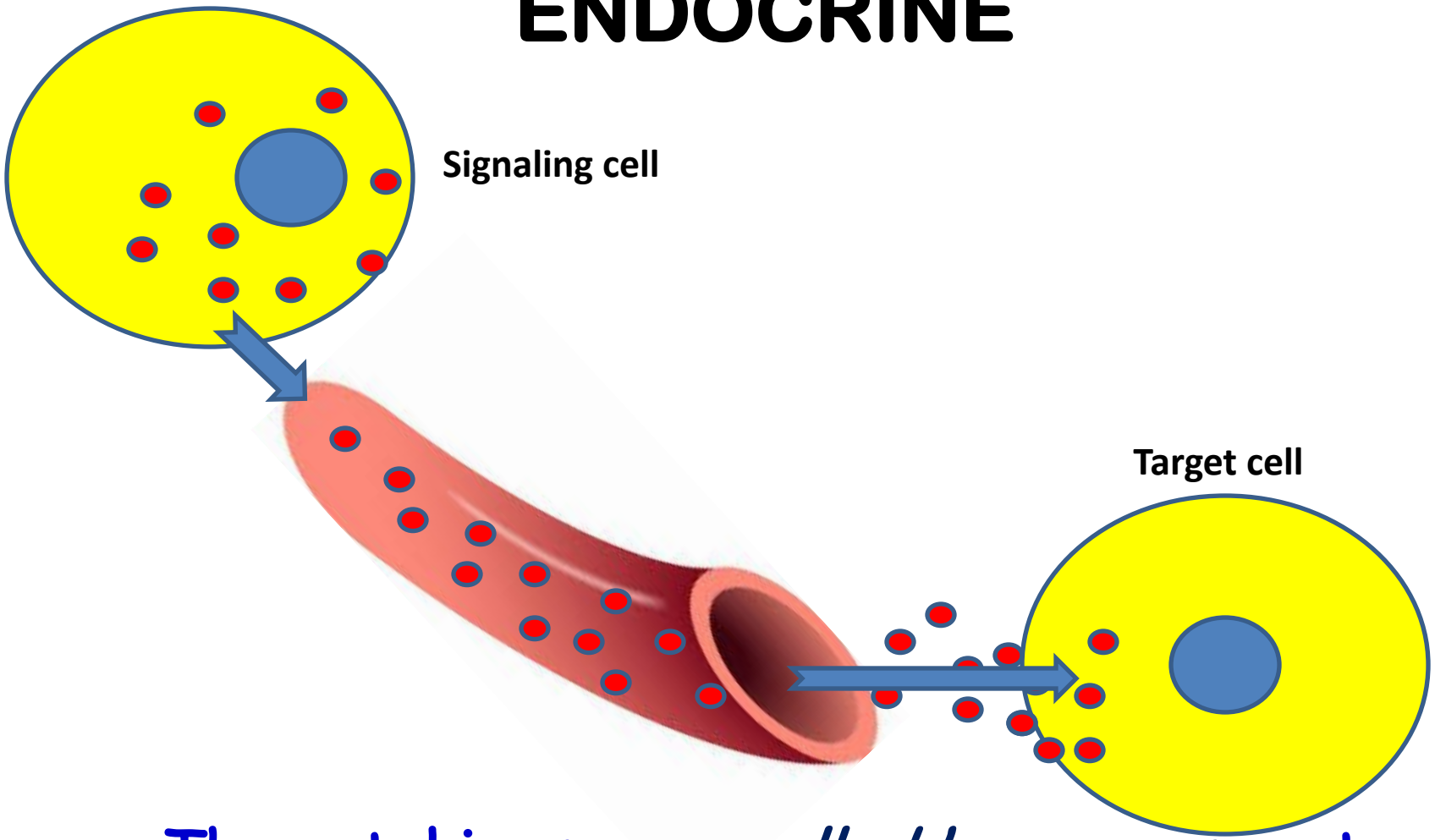
Cytokines include chemokines, interferons, interleukins, lymphokines, and tumour necrosis factors,

But not

hormones or growth factors.

Through Hormones

ENDOCRINE

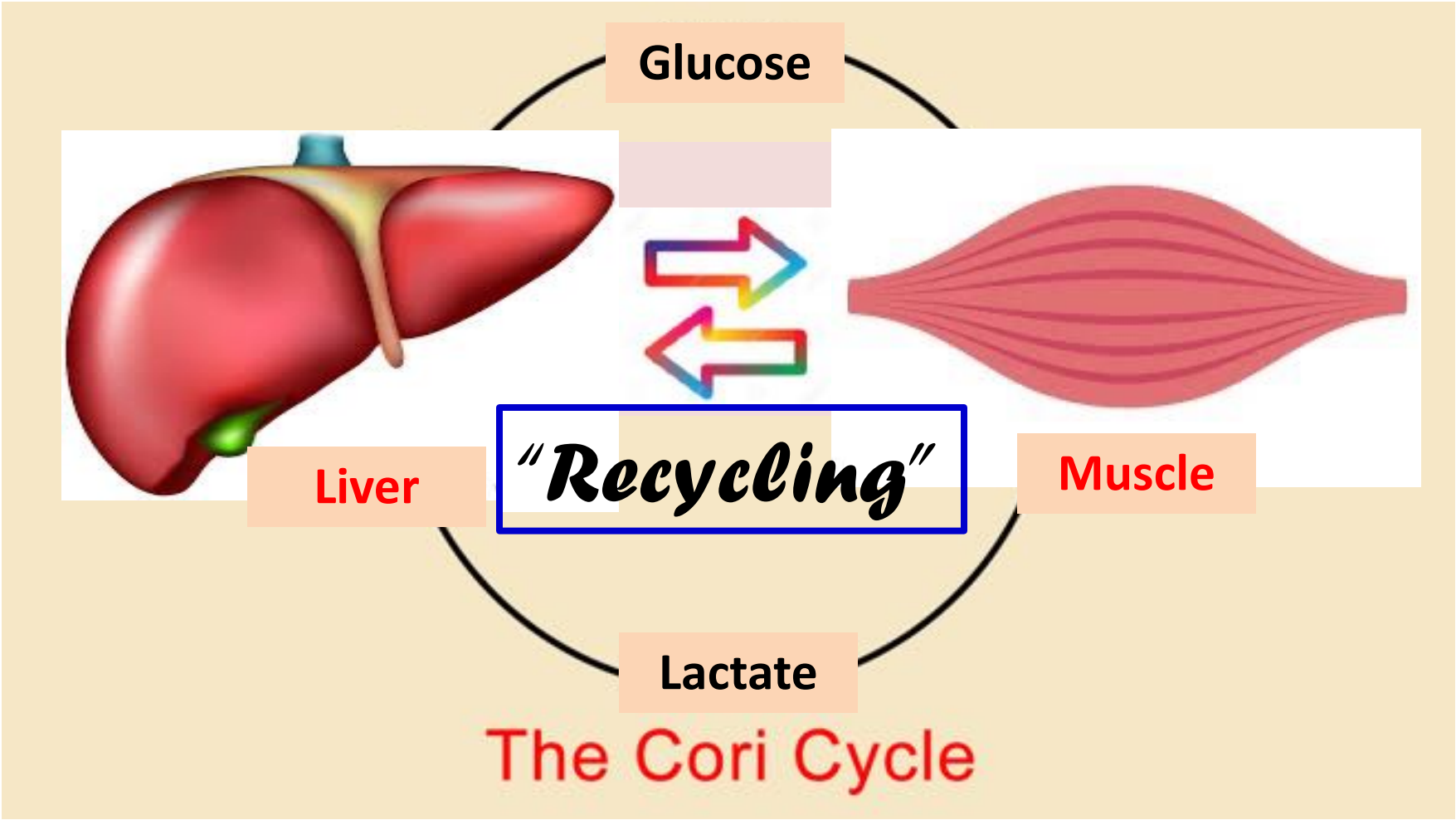


The cytokines, *now called hormones*, go to the blood stream to target distant organs.

Hormones are **your body's chemical messengers** that coordinate different functions in your body by **carrying messages through your blood to your organs.**

These signals tell your body **what** to do and **when** to do it... They work **<u>slowly</u>**, over time, and affect many different processes.

Through Nutrients and Metabolites

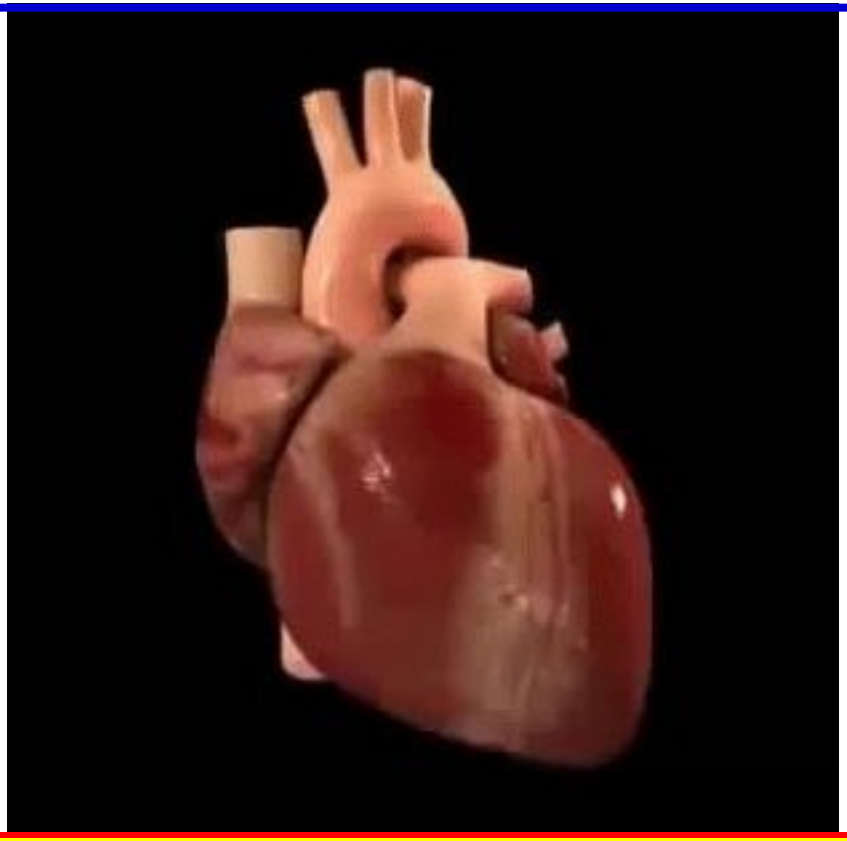


This "Cori cycle" was one of the first described examples of an efficient communication system between organs.

lactate

Another well known example occurs during intense exercise, where lactate is produced in large amounts.

"metabolic flexibility"

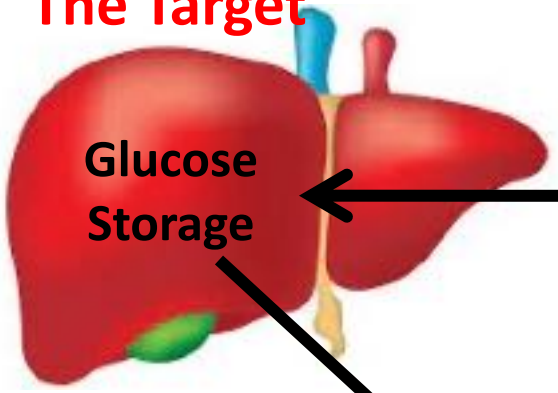


Lactate, *then*, goes back to the heart to serve as the main energy fuel for this actively working machine.

again

Raised Blood Glucose
(The signal)

The Target



Glucose
Storage

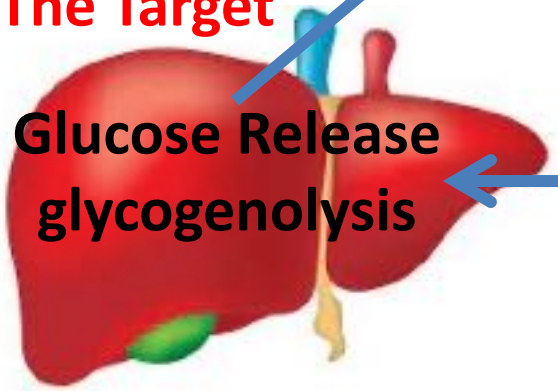
INSULIN

The Target

Lowered Blood Glucose
(The effect)

Raised Blood Glucose
(The effect)

The Target

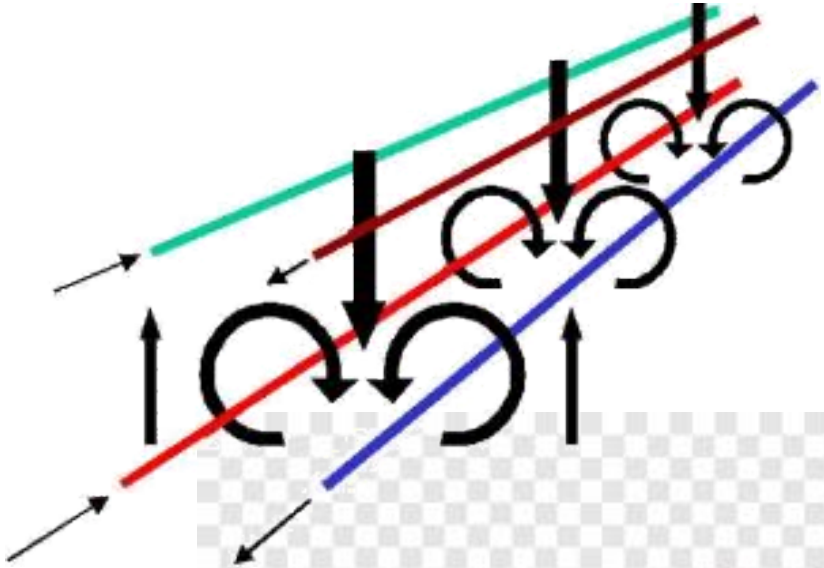


Glucose Release
glycogenolysis

Glucagon

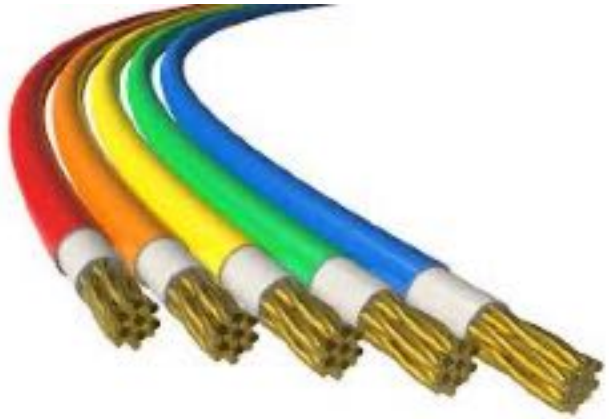
The Target

Low Blood Glucose
(The signal)



As well,

MAY BE,



Along wires and cables

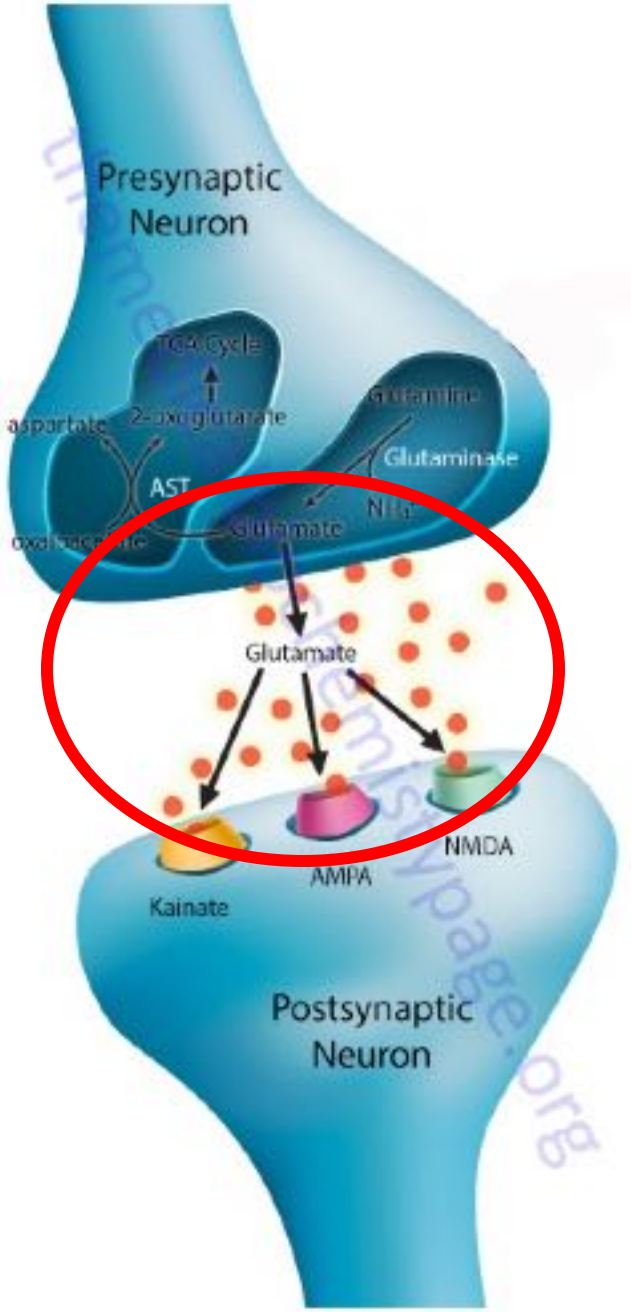
(neurotransmitters via Tracts & Nerves)

synapse

A **neurotransmitter** is a signaling molecule secreted by a neuron to affect another cell across a **synapse**.

Common neurotransmitters known include

Glutamate, GABA, Acetylcholine, Glycine , Dopamine Serotonin, Epinephrine and Norepinephrine.




SŌ

Cross Talks

wires and cables

Wireless

Tracts & Nerves
(Neurotransmitters)

Nutrients and Metabolites

Hormones

Cytokines

Now, how do the kidneys talk to other organs ?

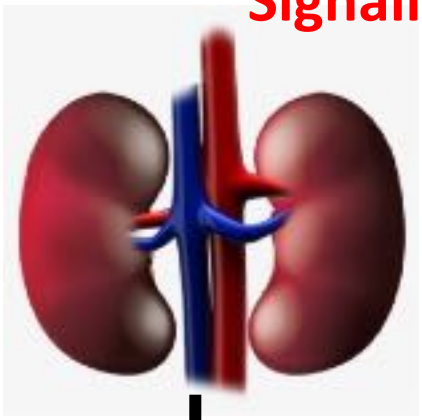
The Kidneys TALK to the rest of the body with

4 SIGNALING MOLECULES;

3 hormones and 1 enzyme

Renin

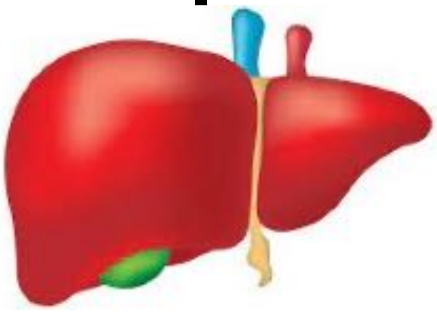
Signaling Organs



Renin

ACE

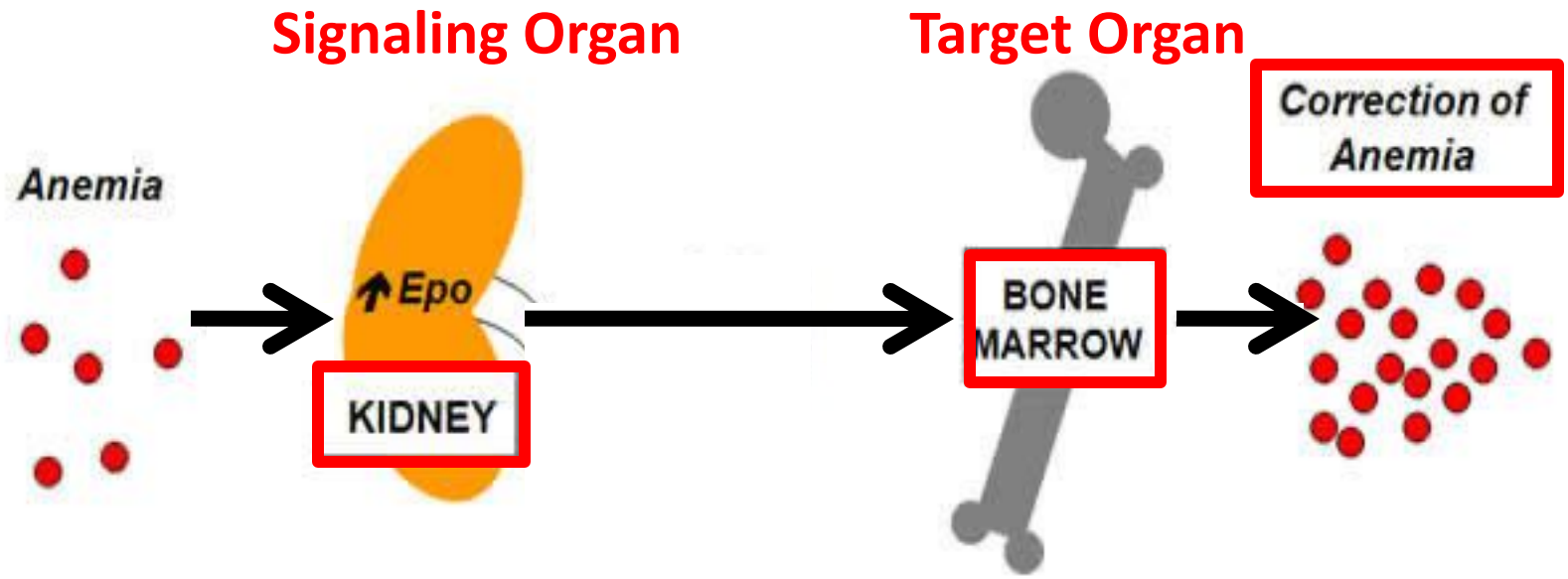
Angiotensinogen → Angiotensin I → Angiotensin II



Target Organs

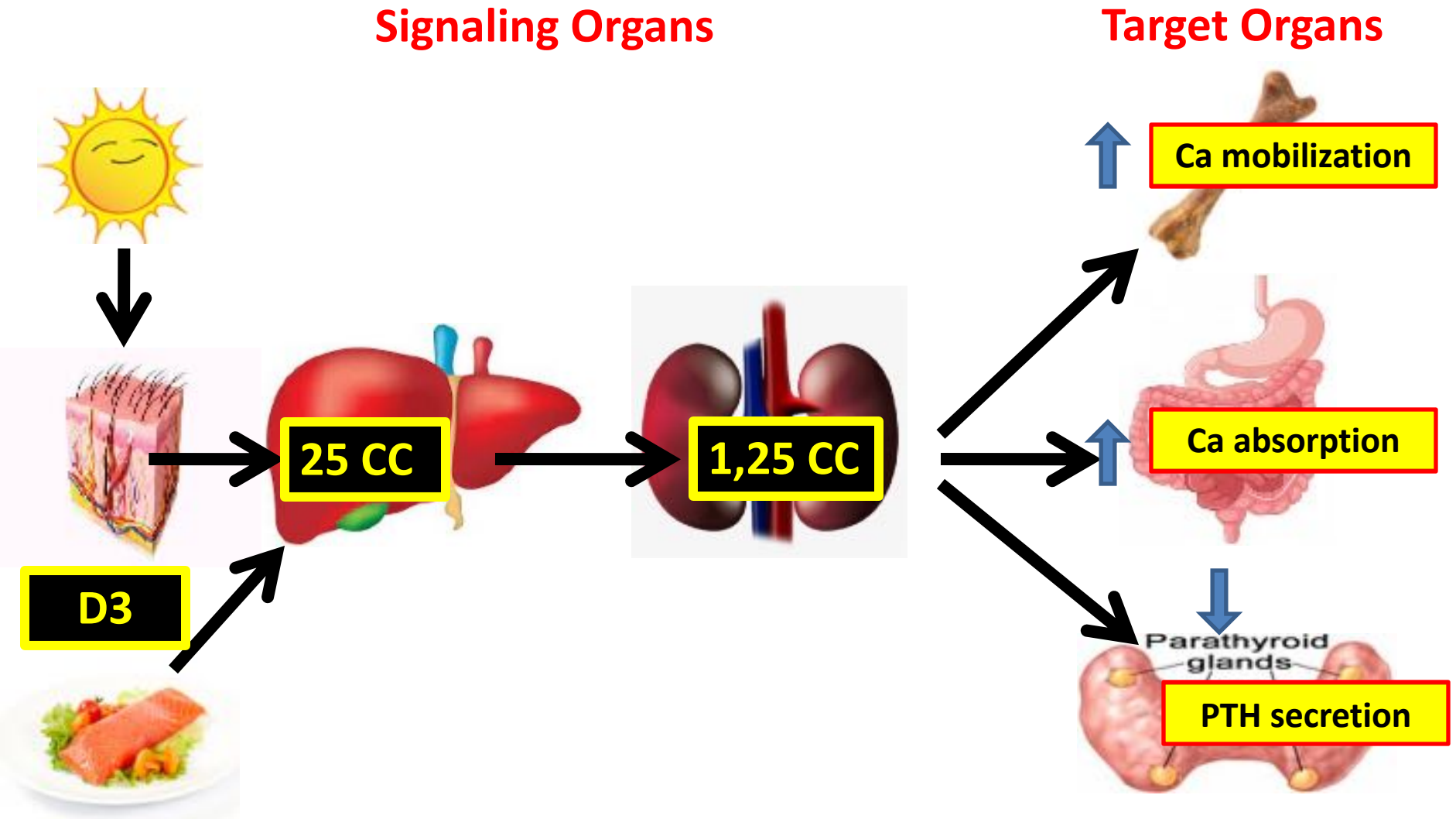
- Sympathetic activity
- Increased Na+ Reabsorption
- Vasopressor Effect
- Increased HR & Contractility
- Aldosterone secretion
- ADH secretion

erythropoietin (EPO)

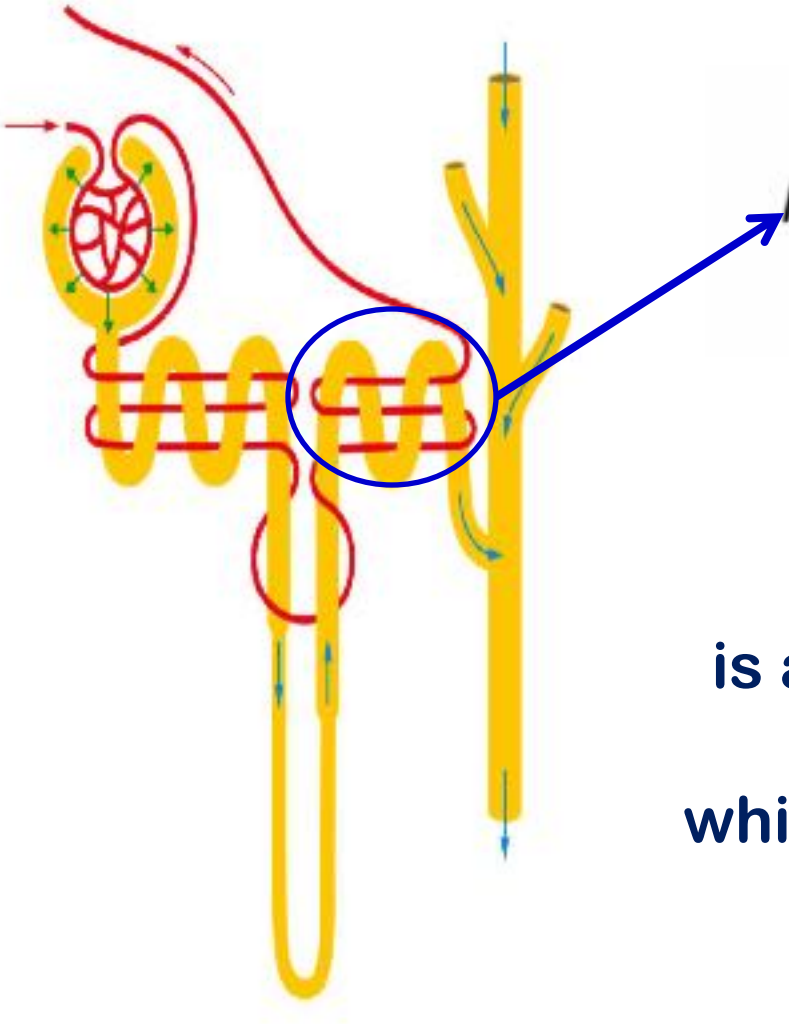


Erythropoietin, is **secreted** by the kidney in response to cellular hypoxia;
it **stimulates** red blood cell production in the bone marrow.
And **correction** of anemia will follow.

1,25 dihydroxy vitamin D3


Signaling Organs
Target Organs
25 CC
1,25 CC
D3
Ca mobilization
Ca absorption
Parathyroid glands
PTH secretion

Kallikreins

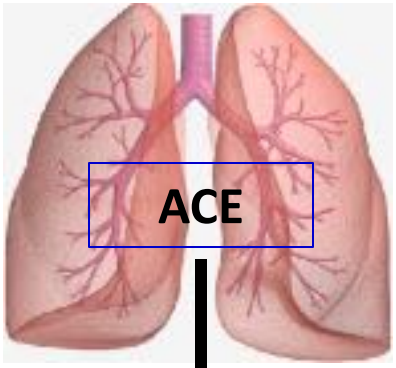


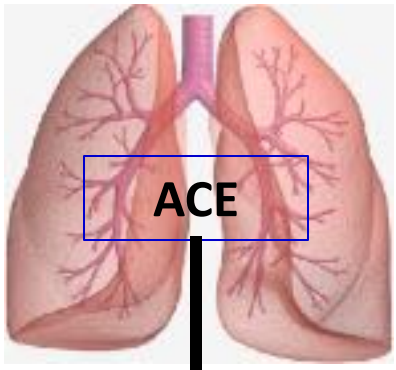
Kininogen

Kallikreins

Bradykinin

Bradykinin
is a potent vasodilator and a diuretic,
which participates markedly in the lowering of the blood pressure.





ACEi

Inactivation of Kinin

Active Kinin

ACE inhibitors prevent the inactivation of kinins and potentiate the actions of kinins by about 50-fold.

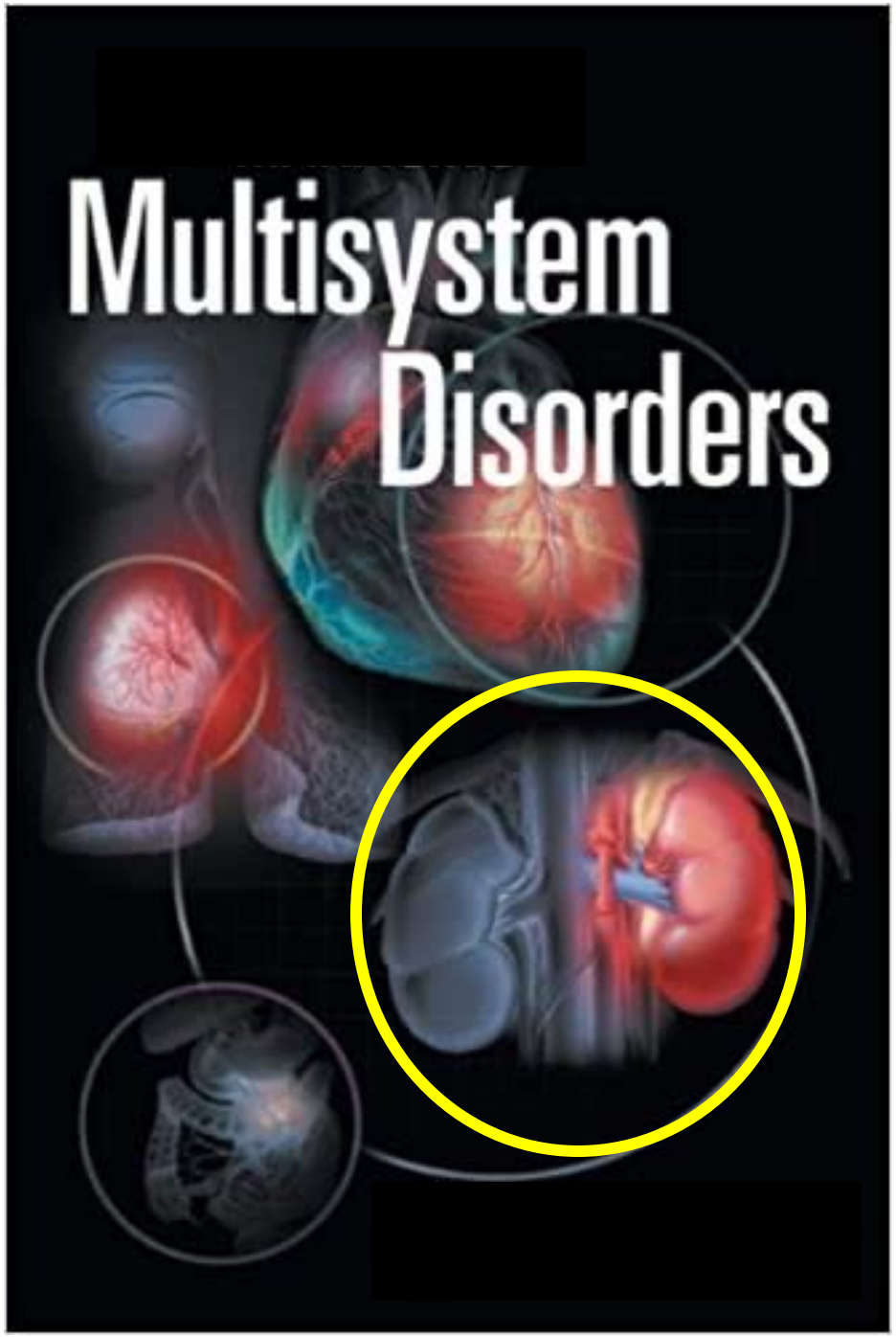
Kinins are involved in the blood pressure-lowering effects of ACE inhibitors.

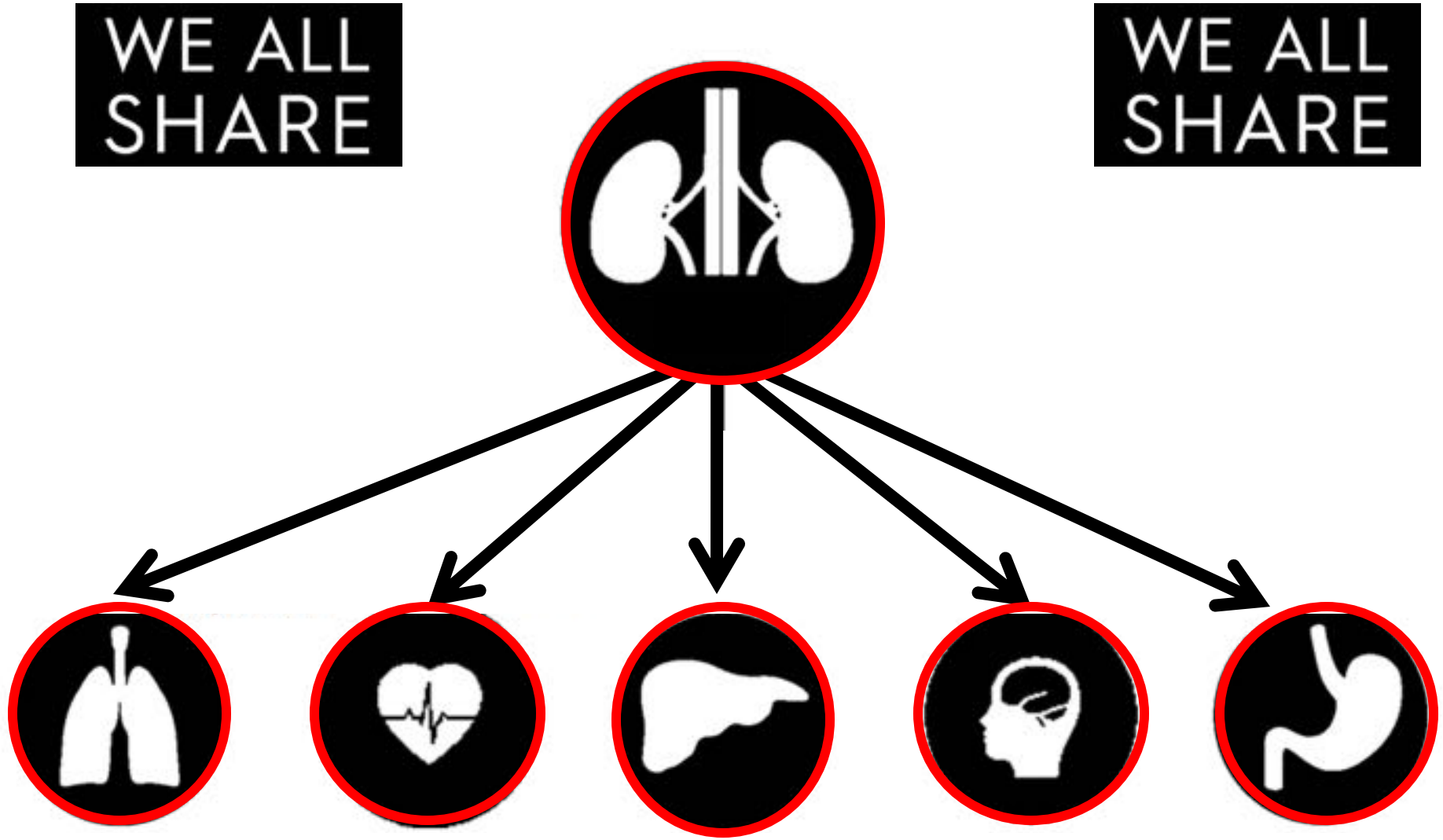
This is one of the reasons ACEi may be superior in the lowering of high BP than ARBs.

ARBs are preferred only for patients who have adverse reactions to ACE inhibitors.

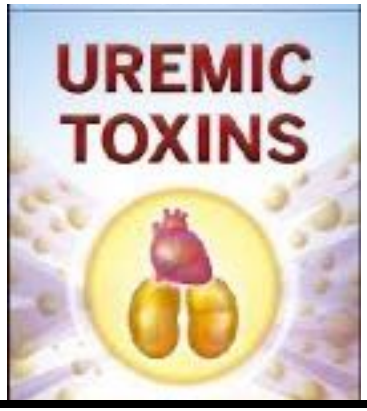

inDisease

A Kidney disease is not just a diseased kidney, it is rather a multisystem disorder with whole body dysregulation and Inter-Organ Cross-Talk



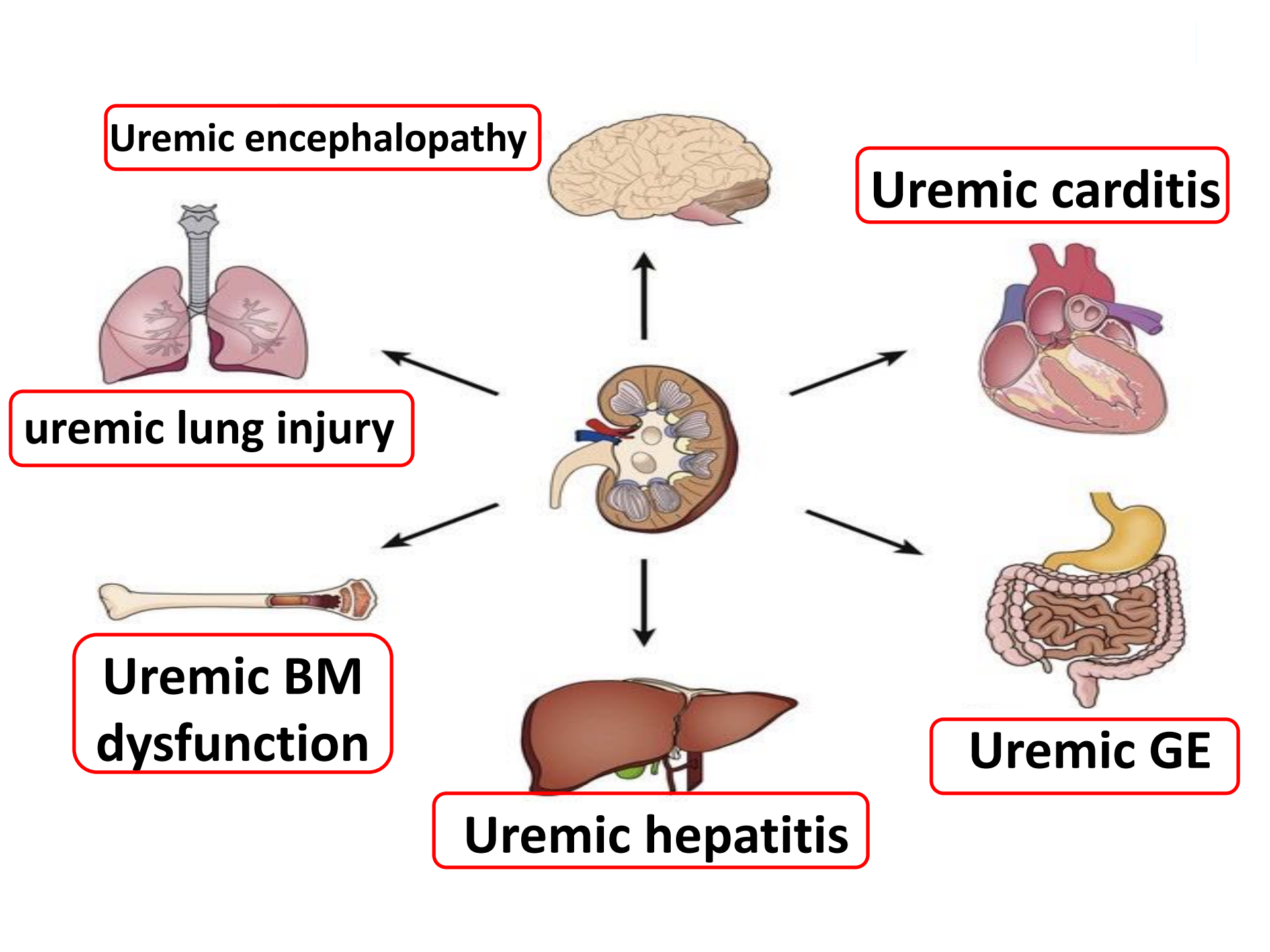


Deleterious **interorgan crosstalk** arises in **kidney disease**, due to the **imbalance** of immune, inflammatory, and soluble mediator metabolism.



The retention of many compounds, which under normal conditions are filtered by the healthy kidneys, leads to the accumulation of *uremic toxins* *and the* development of the uremic syndrome.

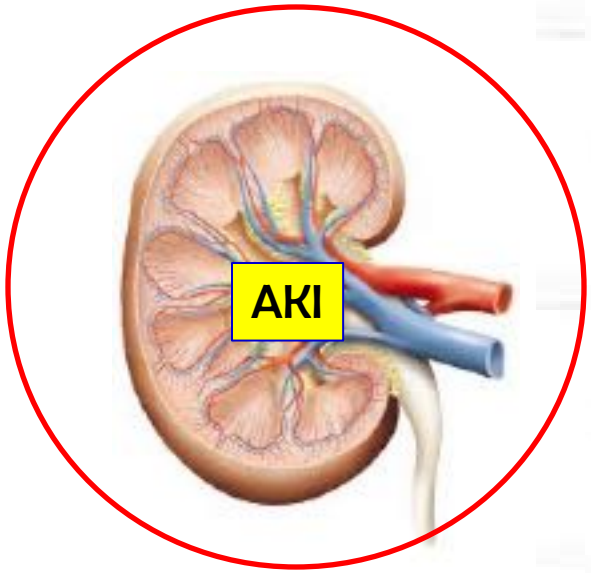
Which may include,

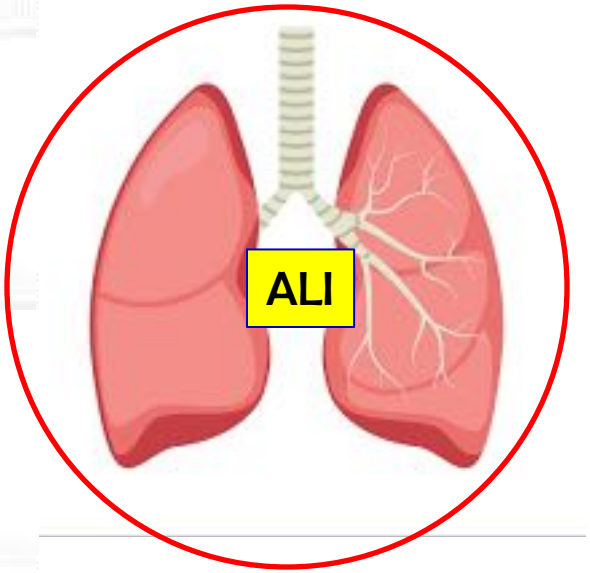

Uremic encephalopathy
Uremic carditis
uremic lung injury
Uremic BM dysfunction
Uremic hepatitis
Uremic GE

And in the remaining few minutes, I will come across 2 famous examples of how the kidney may affect or be affected by diseases faraway in other organs.

Kidney-Lung Cross-Talk

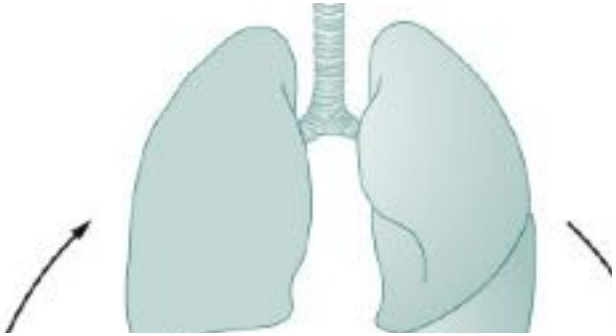
PULMORENAL SYNDROME



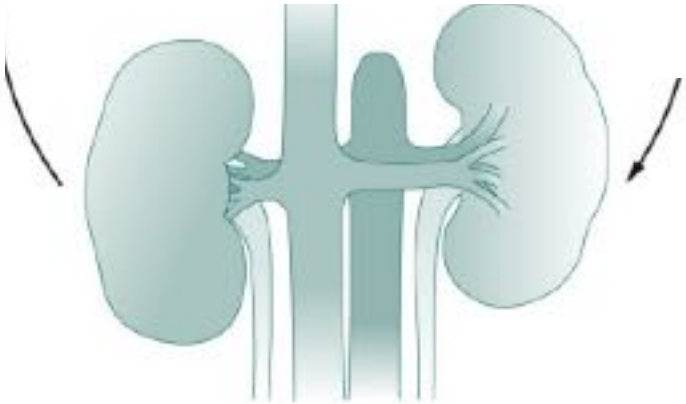


pediatric AKI and ALI are the two most common organ failures we deal with every day in the ICUs.

Acute Lung Injury



kidney–lung crosstalk can be *bidirectionally* deleterious.

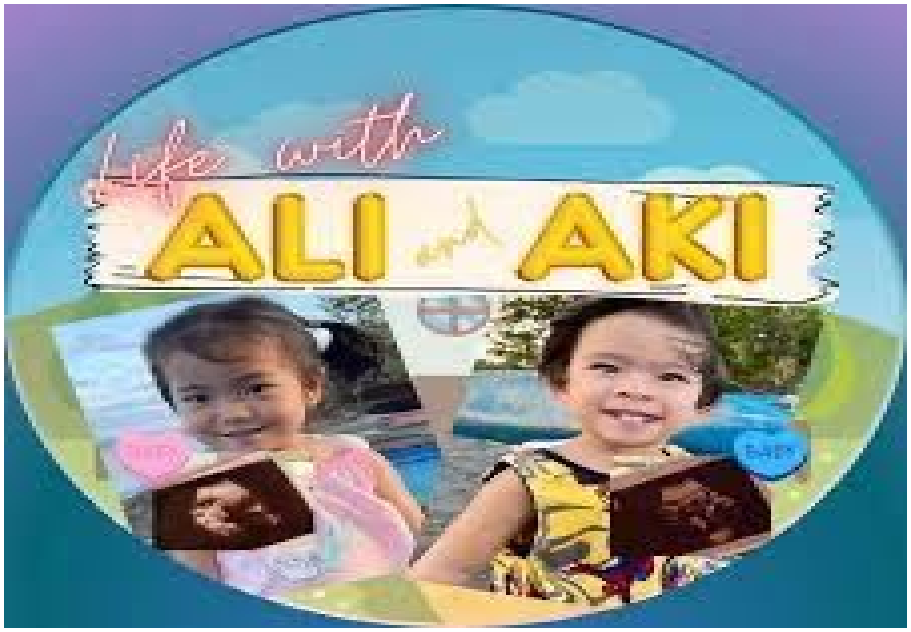


Acute Kidney Injury

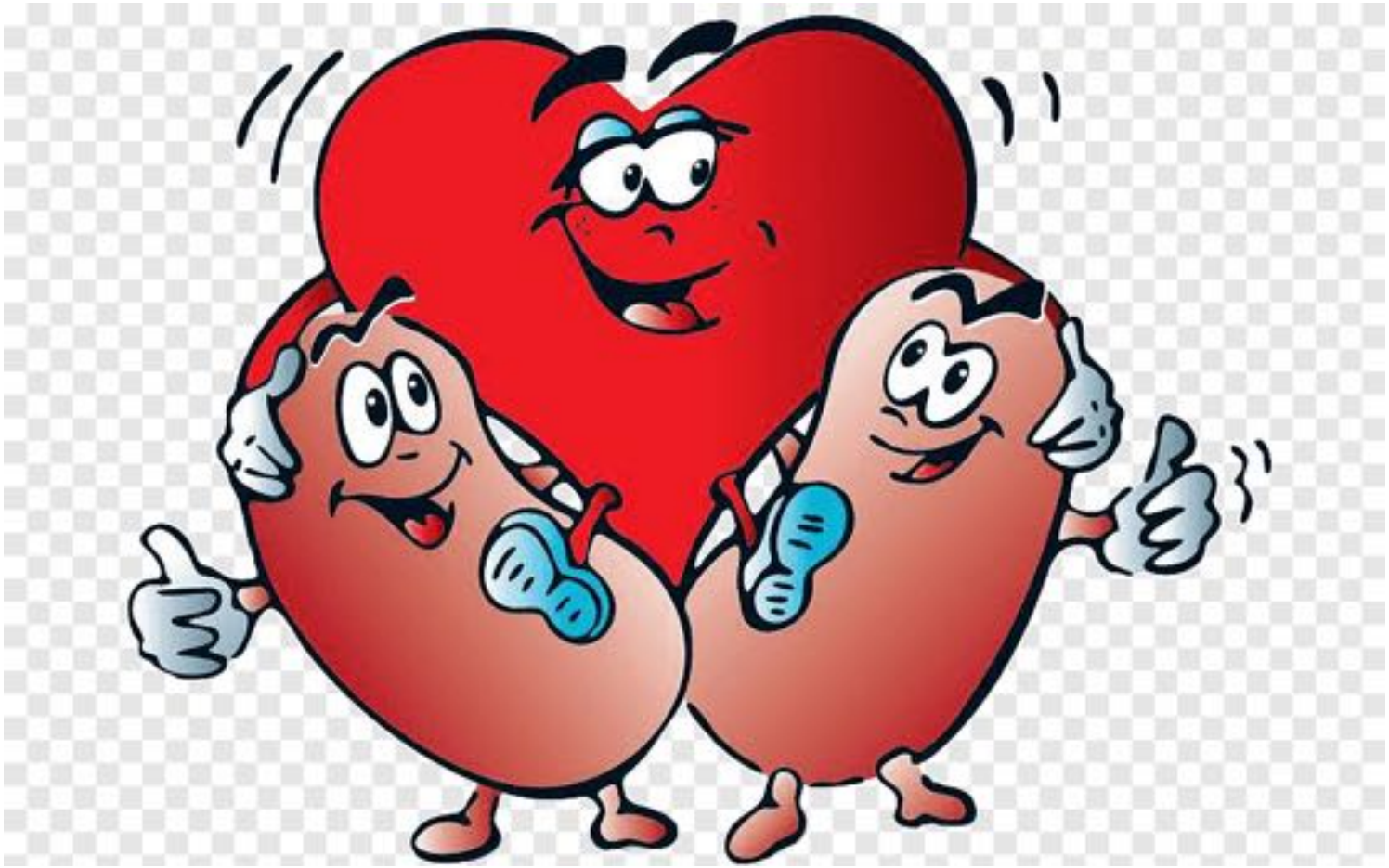
AKI can present with *pulmonary edema* and require *mechanical ventilation*.
Aggravation of the kidney condition may worsen further by *ventilation procedures*.

ALI induces *renal hypoxia and* can cause the kidneys to lose their autoregulation mechanism.
Hypercapnia in ALI causes *vasoconstriction* in the renal vascular network and activation of the RAAS.

Acute kidney injury
is the most common organ dysfunction
in patients with
acute respiratory distress syndrome.

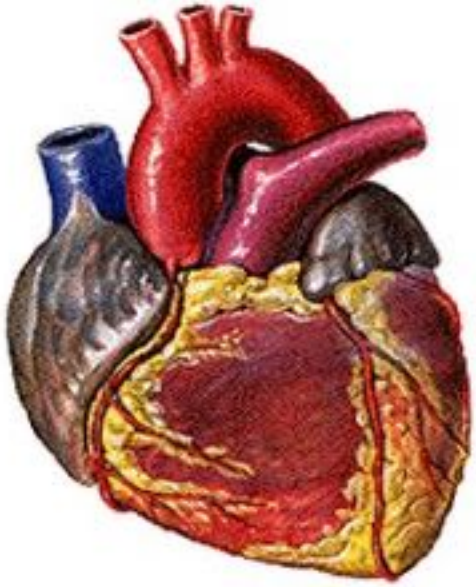


The crosstalk between AKI and ALI remains a major clinical challenge.

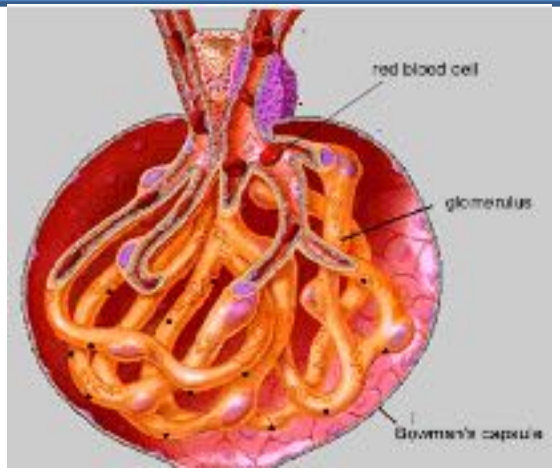


Heart-Kidney Cross Talk

PUMPS



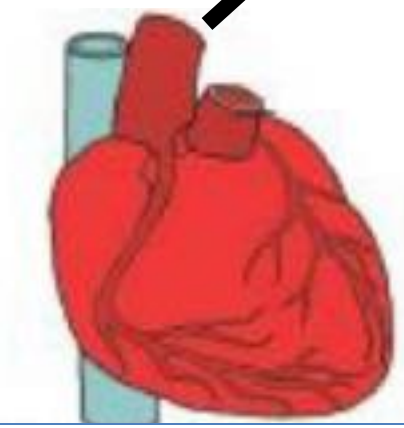
The heart **pumps** blood. The kidneys **clean** the blood. Without the kidneys, your blood would have too much waste. Without the heart, your kidneys would not have the blood to clean or the oxygen to function.



CLEAN

Reduced Cardiac Output

Reduced Renal Perfusion

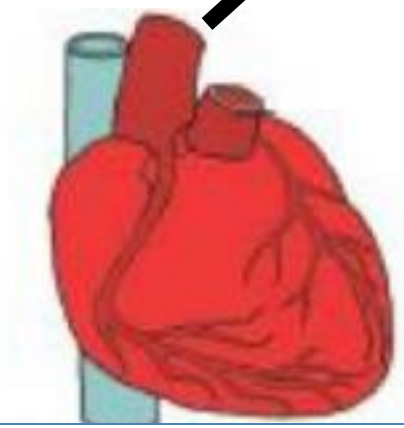


Cardiac Hypertrophy of overload with Failure

Renal Insufficiency

Reduced Cardiac Output

Reduced Renal Perfusion



Cardiac Hypertrophy of overload with Failure

Renal Insufficiency

Reduced Cardiac Output

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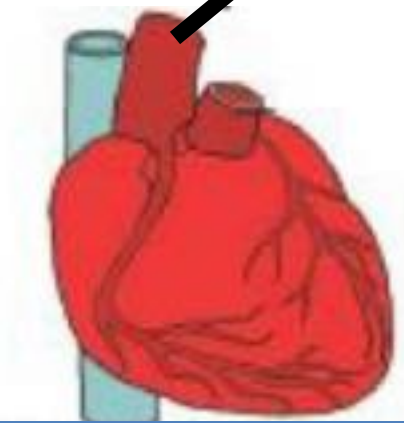
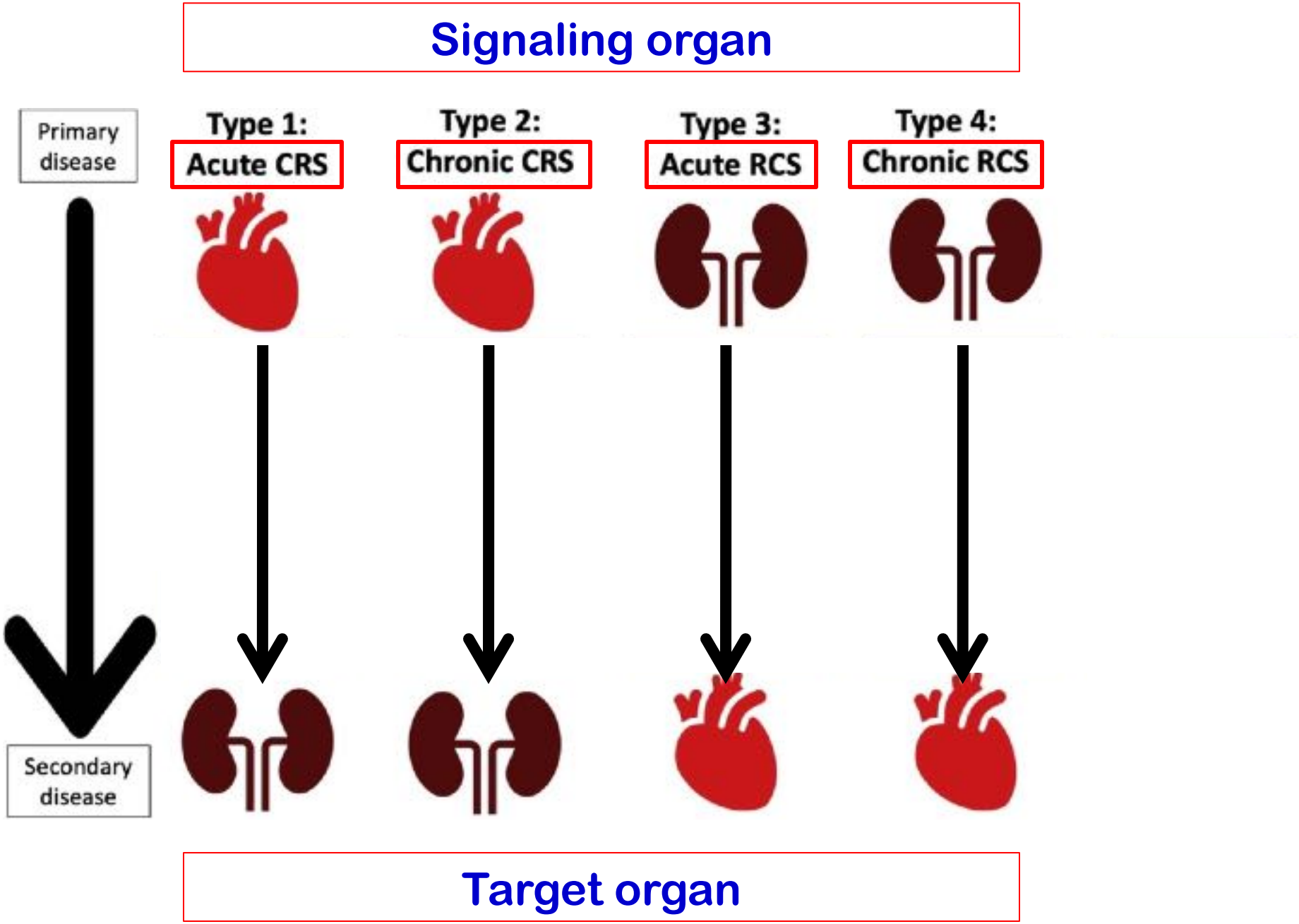
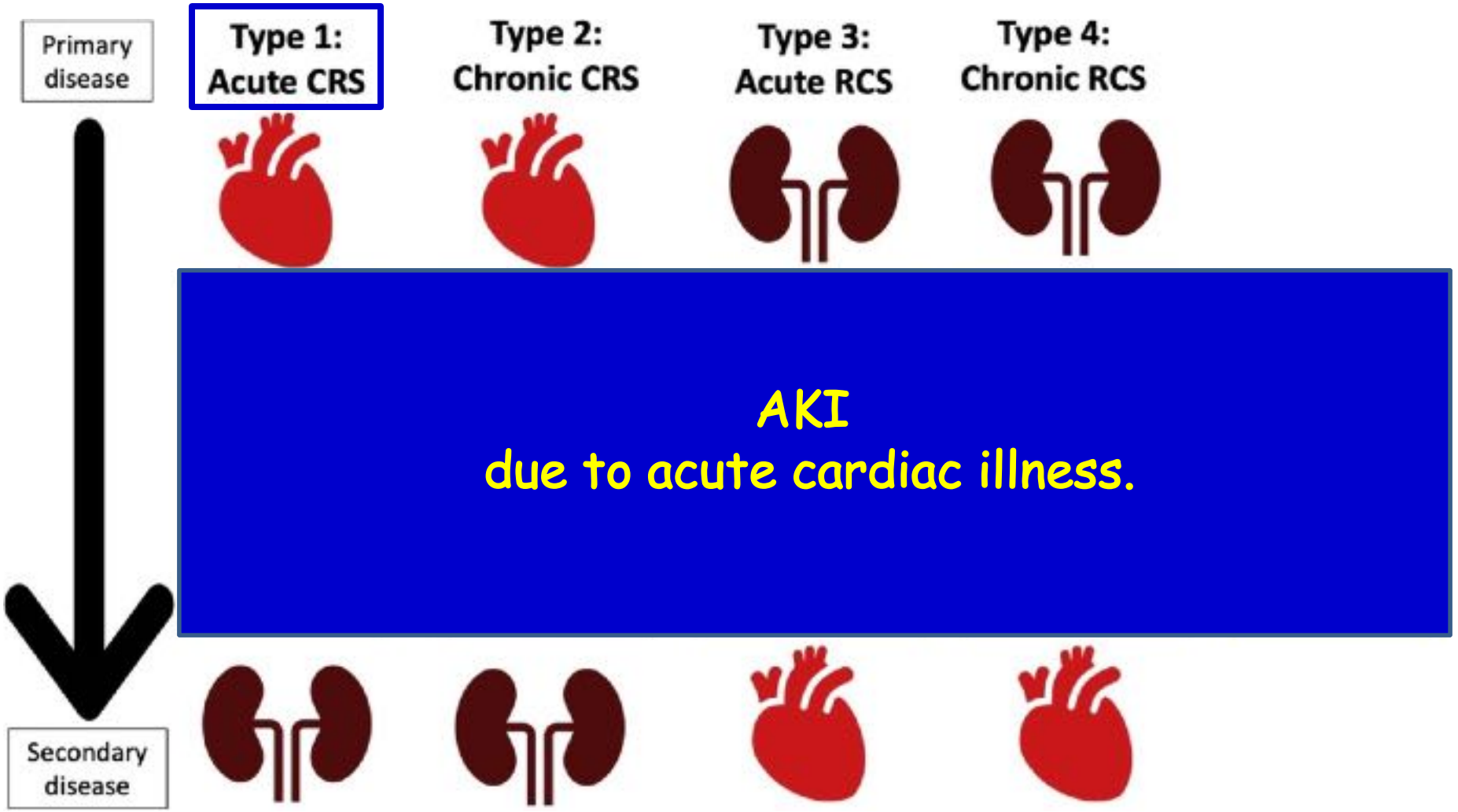
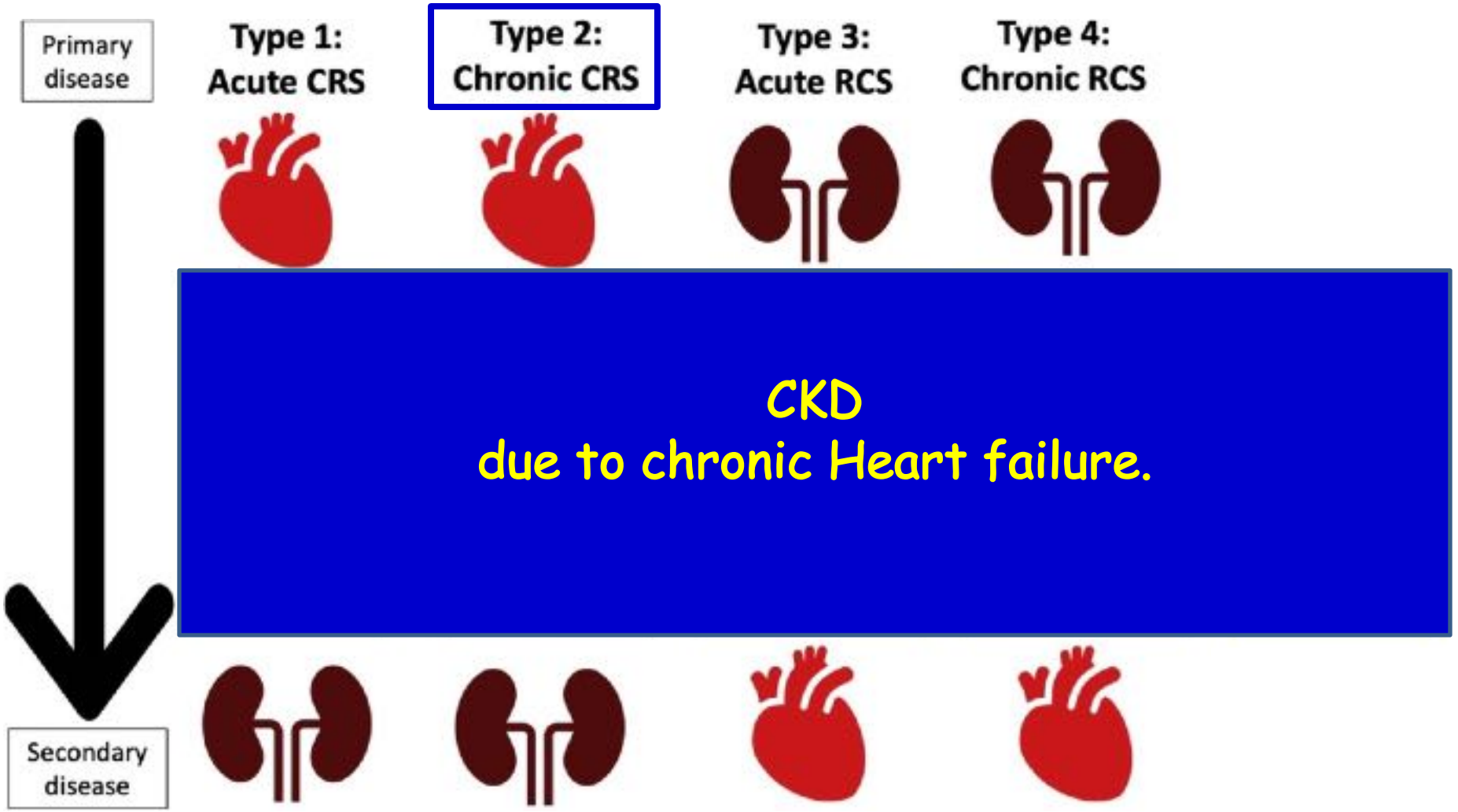


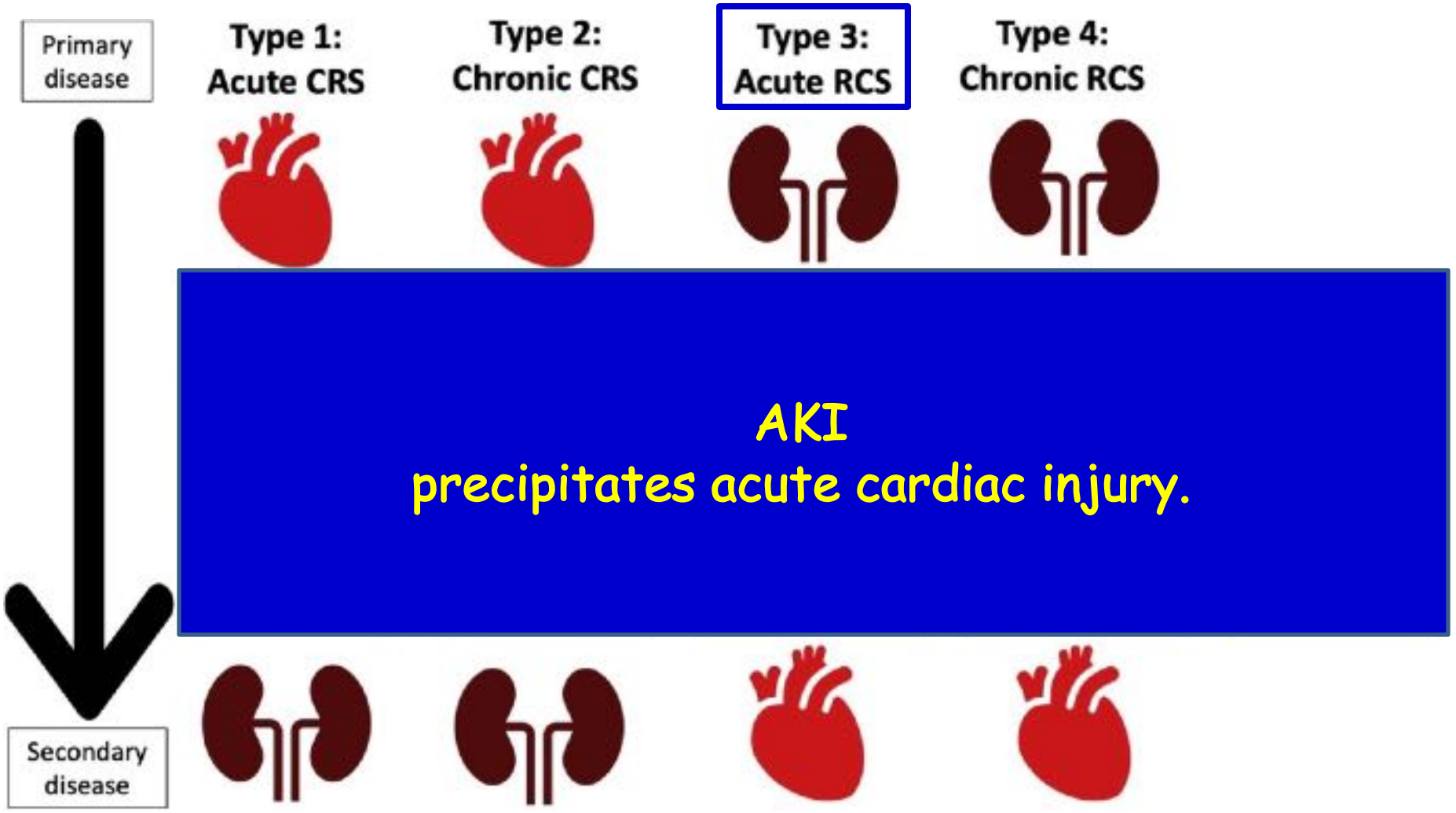
Cardiac Hypertrophy of overload with Failure

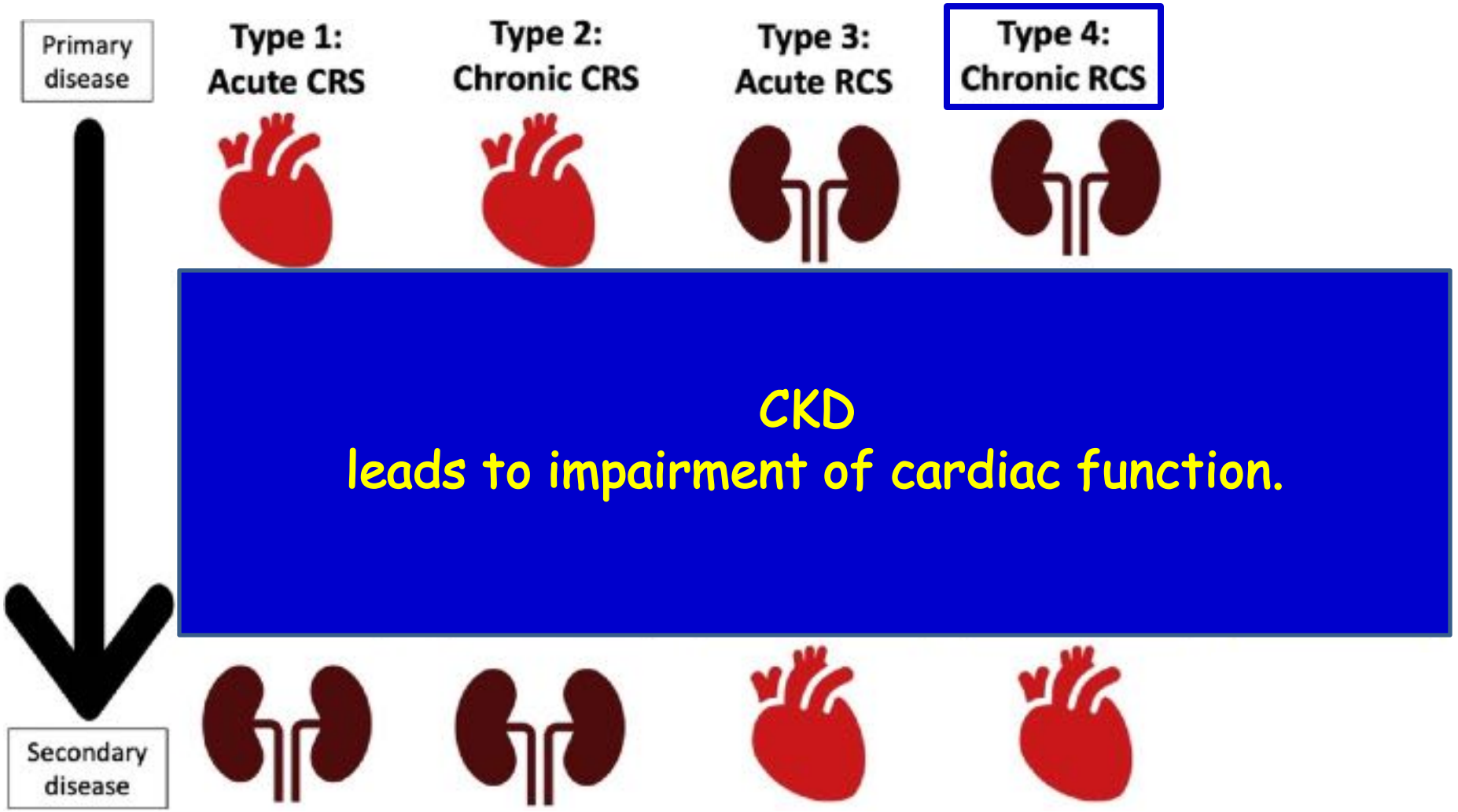
Renal Insufficiency


Signaling organ
Primary disease
Type 1:
Acute CRS
Type 2:
Chronic CRS
Type 3:
Acute RCS
Type 4:
Chronic RCS
Secondary disease
Target organ


Primary disease
Type 1: Acute CRS
Type 2: Chronic CRS
Type 3: Acute RCS
Type 4: Chronic RCS
AKI
due to acute cardiac illness.
Secondary disease


Primary disease
Type 1: Acute CRS
Type 2: Chronic CRS
Type 3: Acute RCS
Type 4: Chronic RCS
CKD
due to chronic Heart failure.
Secondary disease

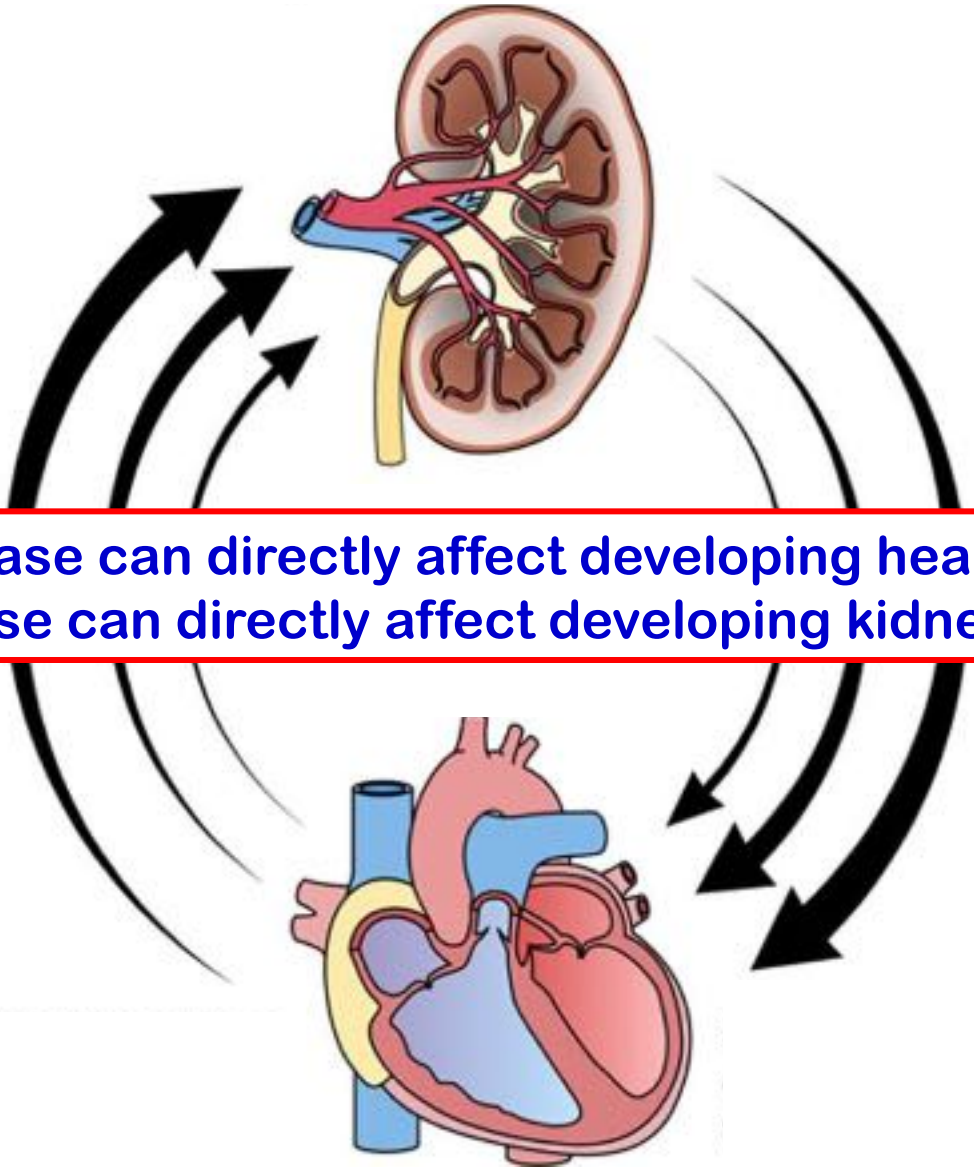

Primary disease
Type 1: Acute CRS
Type 2: Chronic CRS
Type 3: Acute RCS
Type 4: Chronic RCS
AKI
precipitates acute cardiac injury.
Secondary disease


Primary disease
Type 1: Acute CRS
Type 2: Chronic CRS
Type 3: Acute RCS
Type 4: Chronic RCS
CKD
leads to impairment of cardiac function.
Secondary disease

Type 5:
Secondary CRS

In Cardiorenal syndrome type 5
Common pthogenetic patterns exist (i.e. auto-immunity, diabetes, LE, HTN) and both are simultaneously affected.

So...



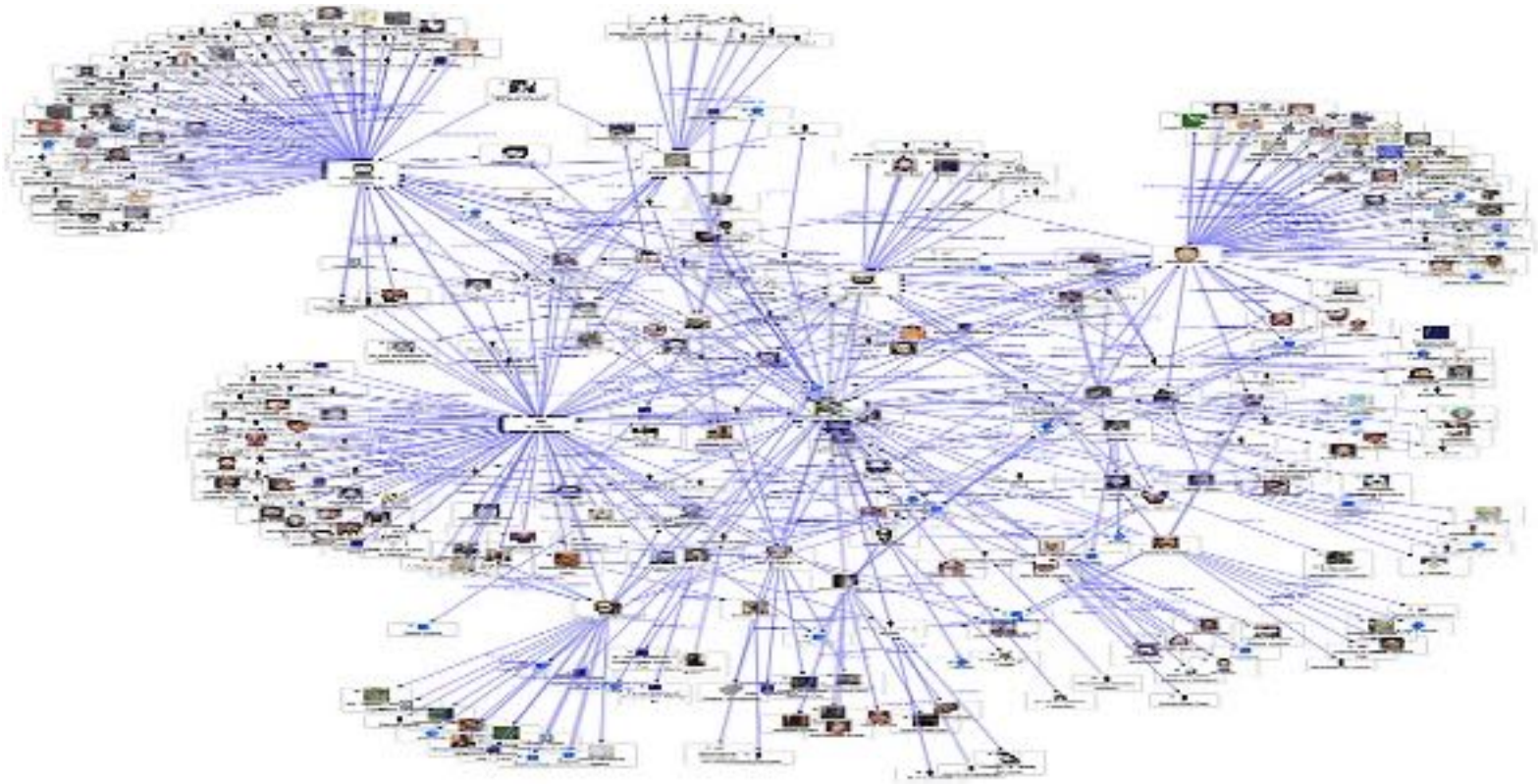
AKI

AHD

Kidney disease can directly affect developing heart disease.
Heart disease can directly affect developing kidney disease.

heart disease is the most common cause of death among people with kidney disease.

Wrap it up !



Interorgan Communication Network (ICN)
is the network of signals that act between organs to coordinate organismal cellular processes under homeostasis and stress.

The signals may be *nutrients, wastes, toxins, metabolites, nucleic acids, proteins, and peptides.*

It is a vast field, and what I went through
in the last few minutes is just
a drop in the ocean

that critical illness is largely a state of

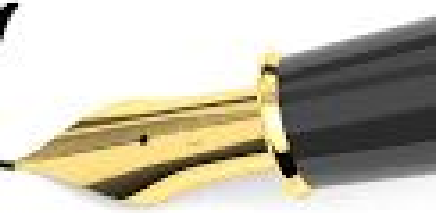
organ crosstalk and interaction

successful management requires a thorough understanding of its nature.

SO,

Please read more, because, understanding of the deleterious organ crosstalk in the critically ill, not only makes you manage better, but as well, provides you a framework for developing novel therapeutics.

Thank you



Ramzi El-Baroudy


MCQs Time

Which of the following part of a neuron receives information from other neurons?

a) myelin sheath

b) dendrites

c) cell body

d) axon

Which of the following cells release insulin when glucose levels elevate in the body?

a) Gamma cells
b) Beta cells
c) Alpha cells
d) Delta cells

Cytokines have important roles in :

a) chemically induced tissue damage repair
b) cancer development and progression
c) control of cell replication and apoptosis
d) All of the above.

The different types of cytokines found in the body include all of the following except:

a) Chemokines and lymphokines
b) Interferons and interleukins
c) Tumor necrosis factors
d) Growth factors