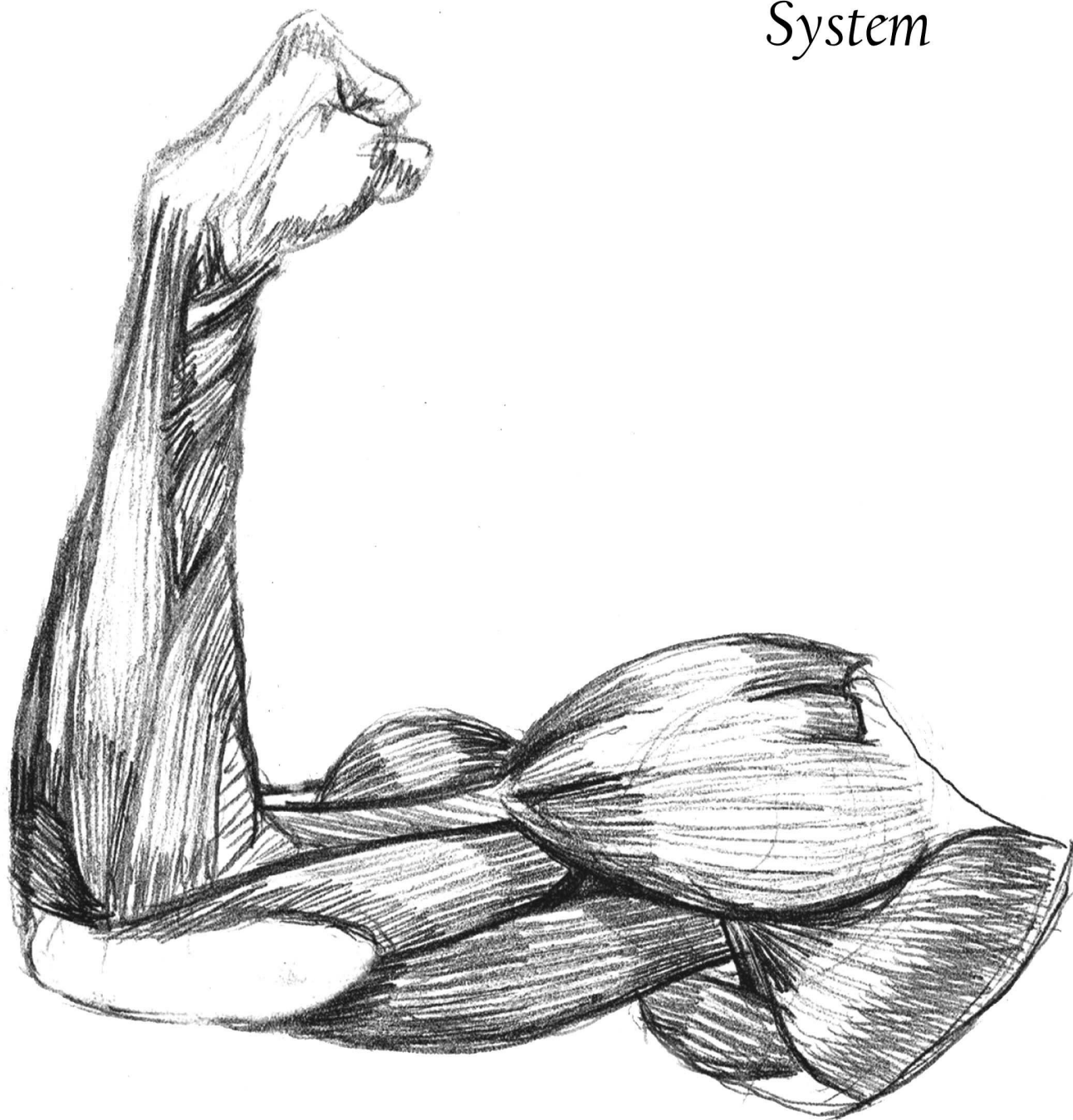


The Skin and
MUSCULOSKELETAL
System



PHARMACOLOGY

SLIDES

SHEET

LECTURE # **1**

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Introduction to MSS' PHARMACOLOGY

- Inflammations

- Inflammations are normal/natural defensive responses in your body to an injury, and then these inflammations are ended by an Anti-inflammatory process.

[An injury: a harmful effect that can destroy normal tissues.]

And this effect (injury) can develop due to either External or Internal causes.

- **External:** e.g:
1. Physical traumas by a knife or car accidents.
 2. Chemical toxicity and burns by gases and acids.
 3. Biological: infections by microorganisms.

And these external causes induce a NON-SELF inflammatory response.

- RELATED STORY:

The doctor and one of his friends were looking for a name of these inflammations that are caused by external microorganisms, he suggested the name "أخماج", but his friend thought that such a name is better given to ruined dead tissues, and they decided to call it: microbial inflammations "الالتهابات الجرثومية" to differentiate them from the "التهابات رثوية".

- **Internal:** e.g: endogenous substances may induce an abnormal inflammation and anti-inflammatory reaction; it's considered a SELF-RESPONSE for the causative agents are actually normally found in the body.

So here the body is fighting itself with an abnormal responses.

An example of this Autoimmune diseases:

- **Rheumatic Arthritis** (Rheumatoid) disease: , where the body starts to recognize some agents as antigens, and produces some antibodies against it, what results in a pathological processes, disability, fever, hyperpyrexia (high fever), and pain in joints.

We need to overcome these symptoms and causes in pharmacology. (:

- And what occurs after inflammation normally? **REPAIR**

We usually establish the inflammatory process to help the injured and damaged tissue to repair.

If there is for example an invasive pathologic microorganism, then we'll use anti-microbial agents (anti-inflammatory) to remove it.

Then **HEALING** that may be complete or incomplete, depending on the type of inflammation.

→ **Symptoms and Complications?**

- **Functional disabilities** as a result of the process of inflammation in joints, [mainly in large joints, and in some small joints as well, e.g: hand, wrist, elbow joints as well as the spinal cord.]

→ Joints deformities.

→ Stiffness.

→ Twisting of body, if the injury affects the spinal cord.

Let's go back to the story of Rheumatoid disease.

- It may affect the knee joint.
- The knee joint consists of bones, cartilage, endothelial membrane, and synovial fluid inside a synovial cavity [the most common site in which Rheumatic Arthritis occurs].
- The synovial fluid – in normal cases - contains main nutrients for cartilage and bone, and maintains healthy articulation and normal movement of joints.
- The problem begins when the body, mainly in old people, recognizes some parts of the synovial fluid as foreign bodies and starts to fight them via immune system.

→ The immune reaction is mediated mainly by WBCs in the area of joint (synovial fluid + cavity), stimulates the T-Cells, Monocytes and **Macrophages** particularly. They all function to start an inflammatory reaction by releasing pro-inflammatory substances from the recruited macrophages. Then follows the release of autokoids (Which are biological factors that have short duration) like **Cytokines**, interleukins, and tumor necrotizing factors, which all affect the synovial fluid, membrane, bone and the cartilage of the joint.

→ The other process is initiated by **B-lymphocytes** that stimulate the release of **Rheumatoid Factors** (inflammatory remarks in the serum to diagnose the disease accurately).

Kindly Remember:

- We mentioned before that the exogenous substrates produce antigens.
- Endogenous products induce the release of **Auto-antibodies** (Self mediated reaction).

Later on if Allah wills, we'll be talking about other substances that participate in the inflammatory process, and the following sequences in the body, including the role of inflammatory cells and cytokines in causing an inflammation that's localized at the area of the joint. However, it may reach other organs and parts resulting in new inflammations in the heart or kidneys with certain bad side effects.

- Brief introduction to the coming lecture

Cytokines: substances released by WBCs and have:

1. LOCALIZED effects: effects in/outside/around the joint.

- Mainly affects the synovial fluid that nourishes the joint, also affects the endothelial membrane that covers the synovial cavity, the cartilage above the metaphysis of the bone and the bones themselves.

→ But, What usually happens to the endothelial membrane?

Inflammation and damage, characterized by an increase in numbers of capillaries with their diameters (dilation) → (redness), swelling of the joint, pain, and hotness (due to the inflammatory process).

→ **What about the cartilage?**

We know, the cartilage mainly consists of Chondrocytes, they're cells which maintain the normal configuration of cartilage and its defined thickness which is important.

Unfortunately, the inflammation is responsible in narrowing and reducing the thickness of the cartilage which restrict the movement, resulting in stiffness and development of some sort of threads of fibers at night.

* And here you'll notice how your patient wakes up at the morning feeling the pain, but when he starts to move, the pain will gradually reduce in severity as these fibers break down.

Also, affected chondrocytes increase the production of proteolytic enzymes that aid in the degradation of cartilage by collagenases and metalloproteinase, narrowing the joint space, allowing friction on the surface between bones that results in severe pain and stiffness.

→ There are cells, we call them **Osteoclasts**, that regulate the degradation of the minerals in the bone and the bony tissue itself.

If an increase in the activity of these osteoclasts occurs, then the patient will be suffering from demineralization and general weakness of bones around the joint.

→ The release of Histamine, Kinin, Prostaglandins, Hyaluronidase, and other enzymes along with Cytokines participate in the inflammatory (pathological) reaction in the endothelial membrane, cartilage, and bone, inducing hotness, redness, disability, disruption of movement and more pain.

2- **Generalized side effects** appear at the heart, lungs, kidneys, or liver.

Let's discuss what happens to the **liver** :

When we take a blood sample to diagnose the disease, we'll notice high levels of proteins (markers) that are usually released from the hepatocytes [e.g: C-reactive proteins, proteolytic enzymes, collagenases, metalloproteinase] , and this is due to the injury and inflammation that affect the liver cells.

We really need to know the pathology of a disease, then we'll understand the pharmacology and the tools that can be used to treat it.

RELATED STORY:

25 years ago, the doctor was talking in an interview about a new drug at that time called "Oraflex". Some companies introduced it to the markets in US and Europe (that's stage 4 in preparing drugs), then after 2 months, a pediatrician in Alabama, Georgia went into a renal shock, and he then recognized the relation between this anti-inflammatory drug and the renal shock.

He became sure from this thought after another 75-years old women was suffering from the same complications.

→ At that time, the company paid 130 million dollars to develop this drug, as the marker for the anti-inflammatory drugs is very huge. Then they dealt with the markets and pharmacies to sell the drug in 2 months before the FDA withdrew it, and it was sold again in 130 million dollars. This was called the story of 130. But sadly, 75 Americans and Europeans died by a renal shock.

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Then, How to **TREAT** Rheumatic Arthritis?

Until now, there is not one perfect single effective drug to treat this disease and allow the patient to live a normal life without bad side effects, although some new drugs are claiming so. These can be dangerous drugs with fatal consequences.

The lines that we are working on involve:

1. Reducing or modulating the inflammatory process by anti-inflammatory agents (NSAIDS) : Non-steroidal anti-inflammatory agents.

→ We'll not talk about the steroidal ones because they are mainly considered in the treatment of hormone-related diseases.

2. Reducing or modulating the inflammatory process by immunosuppressive agents.

3. Analgesics: to deal with pain.

4. Healing: and this is difficult, because we sometimes can't repair or even reduce or delay the progression of the disease.

HERE'S THE **END** OF THE LECTURE.

And the doctor is asking you to prepare for the topic of the next lecture which is: the Non-steroidal anti-inflammatory drugs, Like Aspirin.

Nothing left to say, But these beautiful words for the great Sayyed Qotob to remember :

"إنّ كلماتنا ستبقى مِيّنة لا حراك فيها هامةً أعراساً من الشّموع ، فإذا متنا من أجلها انتفضت و عاشت بين الأحياء. كل كلمة قد عاشت كانت قد اقتات قلب إنسان حيّ فعاشت بين الأحياء، و الأحياء لا يتبنّون الأموات."