

INFLAMMATION

L 23 - INTRODUCTION

DR. M. TARIQ JAVED
 PROFESSOR
 DEPARTMENT OF PATHOLOGY
 FACULTY OF VETERINARY SCIENCE
 UNIVERSITY OF AGRICULTURE, FAISALABAD.

INFLAMMATION

□ LEARNING OBJECTIVES

- ✓ Definition of inflammation
- ✓ Overview of cells and soluble mediators
- ✓ Stimuli for inflammation
- ✓ Role of the blood vessels
- ✓ Leukocytes: extravasation and actions
- ✓ Soluble mediators
- ✓ Chronic inflammation
- ✓ Systemic inflammatory responses

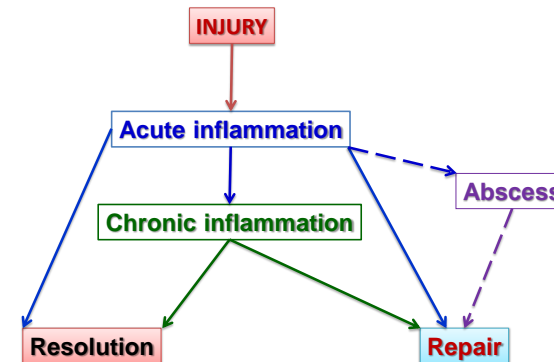
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This Lecture

✓ Concept of Inflammation

- ✓ Definition ?
- ✓ Cardinal Signs ?
- ✓ Name of Scientists?

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- **Burning** or **Set to Fire**, flushing or redness
- Reaction of tissue towards an irritant.
- **Is a stereotyped complex reaction of vascularized living tissue towards a stimulus.**
 - is a complex response to hazardous stimuli (**microbes, toxins, necrotic cells**),
 - occurs in vascularized living tissues,
 - depends on a large number of **chemical mediators**,
 - involves the recruitment and activation of various **plasma proteins and cells**.

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- **If there would have been no inflammatory response, Life would have been difficult**
- Inflammatory process cannot be differentiated from **healing** or **repair** process
 - **Inflammation** is aimed at mobilizing the host defenses to neutralize or get rid off the offending agent
 - the **repair** is aimed at reconstitution of tissue's structural and functional integrity by regeneration or fibroplasia

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Aetiology

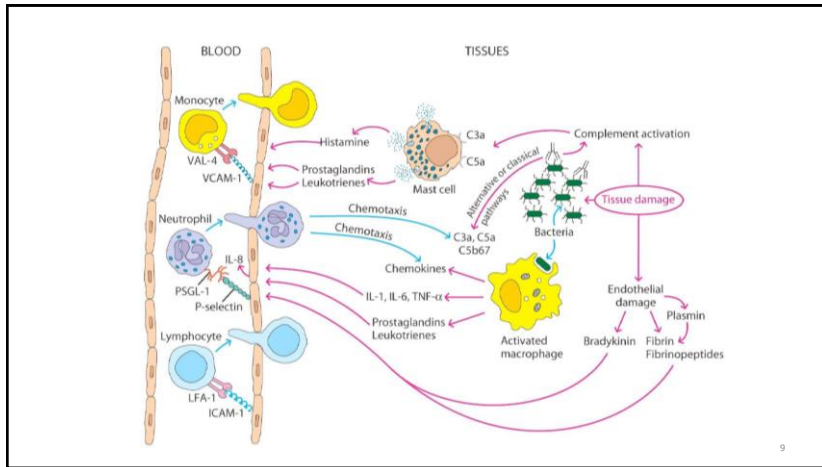
- **Microbial infections:** pneumonia, skin infections, etc.
- **Physical agents:** burns, trauma--like cuts, radiation
- **Chemicals:** toxins and caustic substances like battery acid
- **Others:** immunologic reactions-- rheumatoid arthritis

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SOME GENERALIZATIONS

1. A **complex** process
2. Occur in **living** tissue
3. A **continuous** process
4. An **evoked** response
5. Is **survival** oriented
6. **May cause more damage to tissue**
7. **Stereotyped** (Infl. more of less same process)
8. **Inflammatory components** are all **blood derived**
9. **Highly redundant** (Multiple ways to initiate a pathway)
10. **Surface** oriented

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➤ Inflammation is directed to **dilute, immobilize (sequester), phagocytose** and **destroy** the causative agent.

Cardinal Signs, these were known by Romans

– Heat	– Calor	
– Redness	– Rubor	Celsius (30 BC)
– Swelling	– Tumor	
– Pain	– Dolor	
– Loss of function	– Functio laesa	Virchow (1902)

Added Later

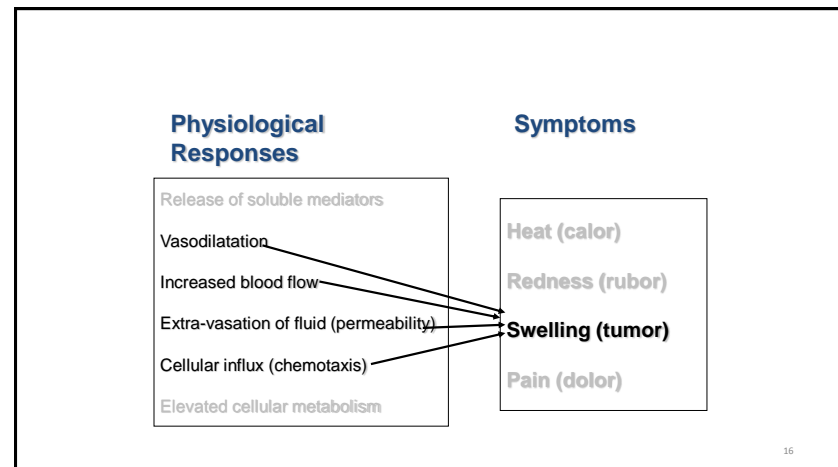
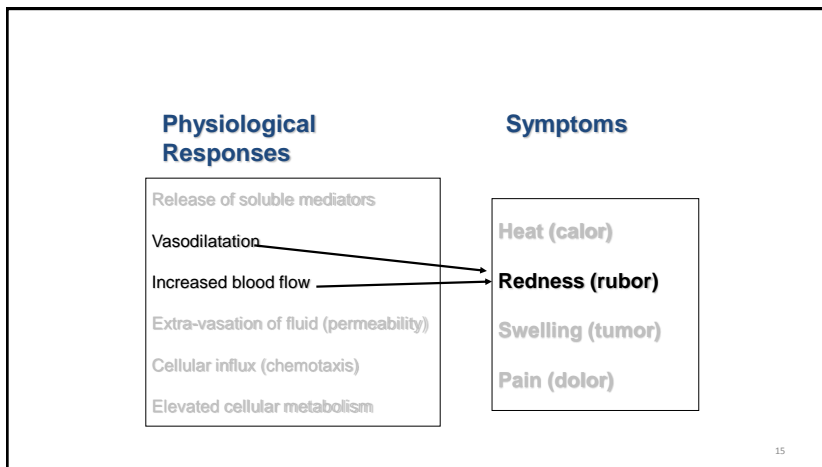
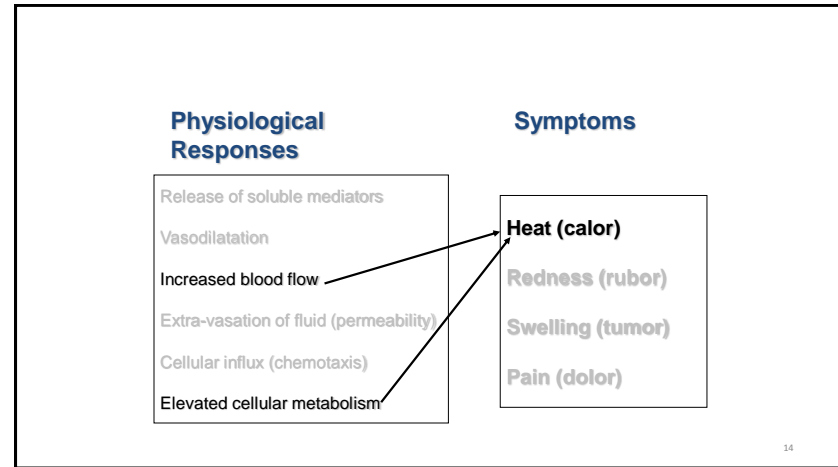
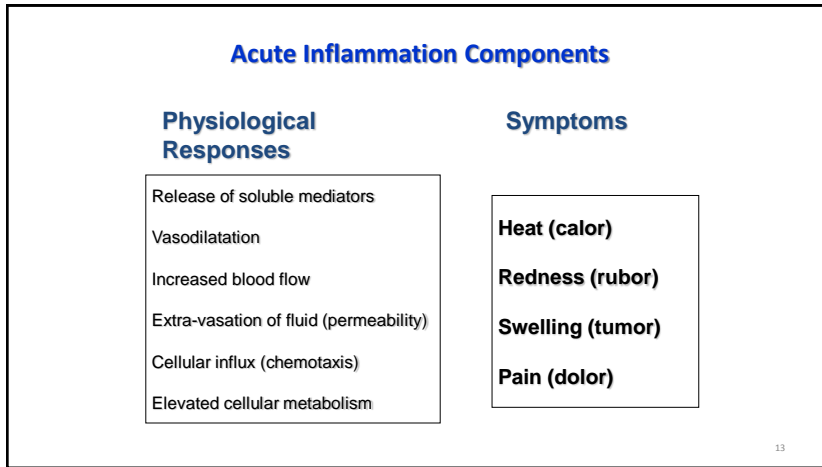
CARDINAL SIGNS OF ACUTE INFLAMMATION

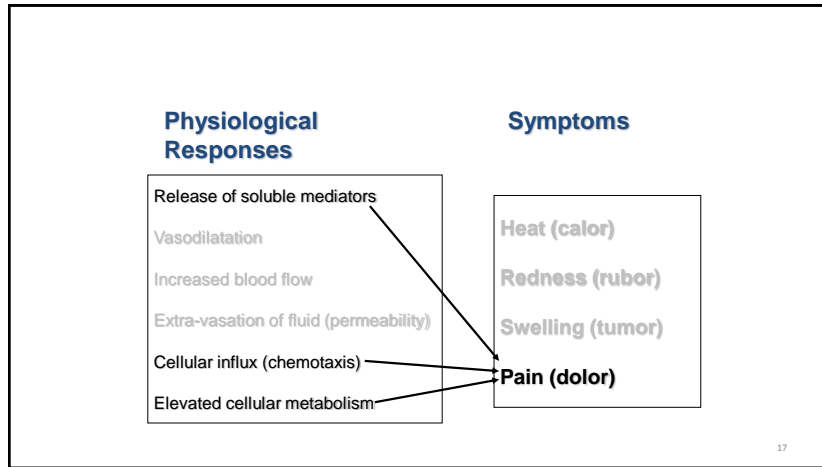
Heat	Redness	Swelling	Pain	Loss of function
Celsius (30 BC)			Virchow (1902)	

Cardinal signs of (acute) inflammation

- **Rubor** = redness
- **Tumor** = swelling
- **Calor** = heat
- **Dolor** = pain
- **Functio laesa** = loss of function

Cellulitis = acute skin infection commonly caused by *Streptococcus pyogenes* or *Staphylococcus aureus*





BRIEF HISTORY

Celsus: 4 cardinal signs
 rubor, tumor, calor, dolor

Virchow: 5th sign
 loss of function

Hunter: “ non-specific response”

Cohnheim: increased vascular permeability

Metchnikoff: phagocytosis

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Stimuli for inflammation

- The molecular stimuli for inflammatory responses are largely “danger signals”,
 - **PAMPs** - Microbial products
 - **DAMPs** - Constituents of host cells expressed during stress or released during necrotic death
- The molecules that act as danger signals activate inflammatory responses by:
 - Binding to membrane **receptors** on cells, thereby activating the cells (e.g., bacterial endotoxin binding to Toll-like receptors)
 - Binding and activation of soluble protein **mediators** of inflammation

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Innate Immune System Receptors (Toll Like Receptor)

TLR structure

Specificities of TLRs

TLR	Ligand	Microbial source
TLR2	Lipoproteins Peptidoglycan Zymosan LPS GPI anchor Lipoarabinomannan Phosphatidylinositol dimannoside	Bacteria Gram positive bacteria Fungi Leptospira Trypanosomes Mycobacteria Mycobacteria
TLR3	? Double stranded RNA	Viruses
TLR4	LPS HSP60	Gram negative bacteria Chlamydia
TLR5	Flagellin	Various bacteria
TLR9	CpG DNA	Bacteria, protozoans

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