INFLAMMATION: EXPLAINED, FRIEND OR FOE?

Anne-Marie Minihane
Prof of Nutrigenetics,
Dept of Nutrition, Norwich Medical School,
What is inflammation??

1. *(Latin, ἰνflammō, "I ignite, set alight")*

2. An essential metabolic process

3. A component of innate (non-specific) immunity

4. A local response to cellular insults that is marked by increased blood flow, capillary dilatation, leukocyte infiltration, and the localised production of a host of chemical inflammatory mediators. It serves to return to homeostasis following injury mediated by an infectious agent, physical damage or metabolic stress.
Innate vs. adaptive immunity

Immune System

Innate (Nonspecific)
1st line of defense
- Cellular Components
- Humoral Components

Adaptive (Specific)
2nd line of defense
- Protects/re-exposure
- Cellular Components
- Humoral Components
What is inflammation?

- (Latin, inflammo, I ignite, set alight")
- An essential metabolic process
- A component of innate (non-specific) immunity
- A local response to cellular insults that is marked by increased blood flow, capillary dilatation, leukocyte infiltration, and the localised production of a host of chemical inflammatory mediators. It serves to return to homeostasis following injury mediated by an infectious agent, physical damage or metabolic stress.
1. Bacteria and other pathogens enter wound.

2. Platelets from blood release blood-clotting proteins at wound site.

3. Mast cells secrete factors that mediate vasodilation and vascular constriction. Delivery of blood, plasma, and cells to injured area increases.

4. Neutrophils secrete factors that kill and degrade pathogens.

5. Neutrophils and macrophages remove pathogens by phagocytosis.

6. Macrophages secrete hormones called cytokines that attract immune system cells to the site and activate cells involved in tissue repair.

7. Inflammatory response continues until the foreign material is eliminated and the wound is repaired.
Inflammation is a complex metabolic process involving the interaction of numerous organs, cell types and a wide array of chemical inflammatory mediators.
Resolution of inflammation is an active process not simply a ‘turning off ‘ of pro-inflammatory pathways.
Chronic low grade inflammation is a pathological feature of a host of chronic diseases.
Inflammation & atherosclerosis, CVD

Libby P, 2002
Inflammation is a driver of the metabolic dysregulation associated with obesity and excess adipose tissue. Inflammatory status in part differentiates the metabolically healthy but obese (MHO) and the typical metabolically unhealthy obese phenotype.

In EU27, ~60% adults and 20% children are overweight or obese.

Obese adipose tissue:
- Adipocyte hypertrophy
- Macrophage infiltration

Production of inflammatory mediators →
Local and systemic inflammation & adipocyte dysfunction →
Metabolic syndrome, insulin resistance, non-alcoholic fatty liver disease, type II diabetes, cardiovascular diseases

30% metabolically healthy obese (MHO)

<table>
<thead>
<tr>
<th>Metabolically Healthy Obese</th>
<th>Metabolically Abnormal Obese</th>
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<tr>
<td>Adipose-tissue metabolism?</td>
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<td>Muscle characteristics?</td>
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- High fat mass
- High insulin sensitivity
- Low inflammation
- Normal lipids
- Low ectopic fat
- High adiponectin

- High Fat mass
- Low insulin sensitivity
- High inflammation
- Dyslipidaemia
- High ectopic fat
- Low adiponectin

NHANES: Wildman P et al., 2008

Figure 2. Age-standardized prevalence of cardiometabolic abnormalities by body size and sex (A, men; B, women). *P < .001 for proportion metabolically abnormal vs normal weight.
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