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### Ischemia Reperfusion Injury and its Effect on the Myocardium

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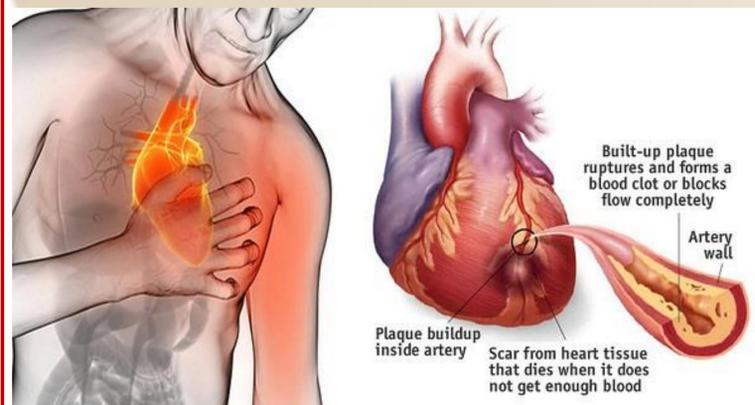
# Ischemia Reperfusion Injury and its Effect on the Myocardium

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## Introduction

- Acute myocardial infarction is a leading cause of morbidity and mortality in the world. Reperfusion strategies are the current standard therapy for acute myocardial infarction (Neri, 2017).
  - Most clinicians assume that ischemic injury terminates with return of spontaneous circulation (ROSC). However, according to Ibáñez 2015, damage inflicted on the myocardium during acute myocardial infarction is the result of two processes: ischemia and subsequent reperfusion (Ibáñez, 2015).
1. Ischemia: the occlusion of blood flow to the tissue can be detrimental to the heart due to its high energy demand (Zhou, 2015).
  2. Reperfusion injury: Reperfusion strategies may, result in paradoxical cardiomyocyte dysfunction and worsen tissue damage. (Neri, 2017).



(80% Of Heart Attacks, 2017)

- Ischemic reperfusion injury typically arises in patients presenting with an acute ST-segment elevation myocardial infarction, in whom the most effective therapeutic intervention is timely and effective myocardial reperfusion (Neri, 2017).
- Reperfusion itself is known as a “double-edged sword” due to the spectrum of reperfusion-associated pathologies (Neri, 2017).
- Ischemic reperfusion injury is an important factor of post-infarction heart failure. The infarct size is therefore the main determinant of long-term mortality and chronic heart failure (Ibáñez, 2015).
- Understanding the mechanisms of ischemic reperfusion injury and the possibility of limiting the extent of necrosis during an ST-segment elevation myocardial infarction is of great individual and socioeconomic value (Ibáñez, 2015).

## Effects of Reperfusion Injury

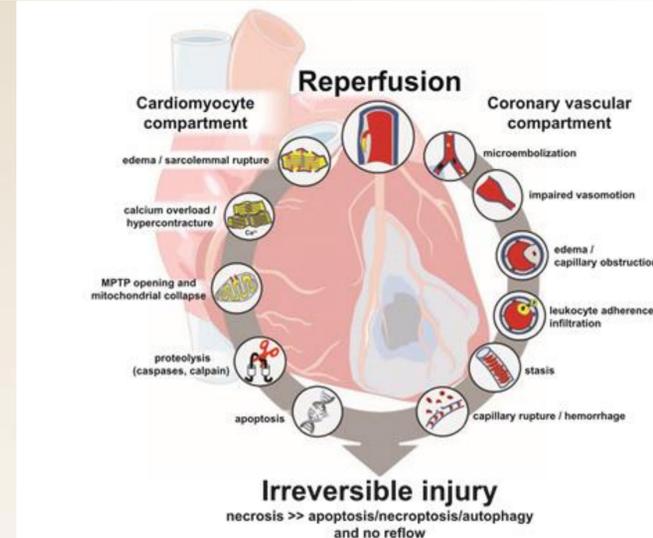
The manifestations indicated below start occurring during myocardial ischemia, but are accelerated with reperfusion.

- Edema, swollen or ruptured mitochondria
- Impaired coronary vasomotion
- Ventricular arrhythmias
- Myocardial stunning
- Leukocyte adherence and extravasation
- Intravascular platelet and erythrocyte aggregates
- Capillary destruction and hemorrhage
- (Heusch, 2017).

## Pathophysiology

Myocardial ischemia reperfusion injury occurs when restoration of blood to ischemic heart reduces cardiac function and causes acceleration of myocardial injury through (Zhou, 2018):

- Reactive oxygen species (ROS): small amounts of ROS offer cardio-protection. However, excessive production of ROS during reperfusion causes injury (Neri, 2017).
- Platelets: thrombocytes are equipped with NADPH oxidase, an enzyme located at a cell membrane catalyzing the formation of superoxide therefore releasing ROS. These ROS are able to induce a reperfusion injury (Seligmann, 2013).
- Inflammation: reperfusion triggers a complex inflammatory reaction accompanied by cytokine release and inflammatory leukocyte infiltration into the endangered myocardial region. This contributes to edema, phagocytosis, proteolysis, apoptosis, and collagen deposition (Jiaqi, 2016)
- Cellular Ca<sup>++</sup> overload: during ischemia, acidosis from anaerobic glycolysis increases influx of Na<sup>+</sup> through Na<sup>+</sup>/H<sup>+</sup> exchange. ICF N<sup>+</sup> accumulation is due to inhibition of Na<sup>+</sup>/K<sup>+</sup> ATPase due to lack of ATP. Subsequent exchange of Na<sup>+</sup> for Ca<sup>++</sup> by reverse mode operation of sarcolemmal Na<sup>+</sup>/Ca<sup>++</sup> exchanger induces ICF Ca<sup>++</sup> overload. Upon reperfusion, the rapid normalization of pH and reenergization in the context of elevated cytosolic Ca<sup>++</sup> induces oscillatory release and reuptake of Ca<sup>++</sup> into the sarcoplasmic reticulum, causing excessive myofibrillar hypercontraction (Ibáñez, 2015).
- Edema: The high cytosolic concentrations of Na<sup>+</sup> and Ca<sup>++</sup> result in ICF edema when ECF osmolarity is rapidly normalized by reperfusion (Ibáñez, 2015).
- Mitochondrial permeability transition pore (MPTP): a large mega channel that opens due to increased Ca<sup>++</sup>, inorganic phosphate, or ROS, all of which are present in reperfusion. Opening results in mitochondrial swelling and ultimately lead to rupture of the outer membrane. (Ibáñez, 2015).



(Heusch, 2017)

- Generation of tissue edema following reperfusion can result in external compression of the microcirculation, reducing the perfusion capacity of the capillary network (Ibáñez, 2015).
- Microcirculation can disintegrate due to prior damage and leak circulating cells into interstitial space (Ibáñez, 2015).
- Hemorrhage: RBC release iron contributing to subsequent inflammatory reaction (Ibáñez, 2015).

## Implications for Nursing Care

Pharmacological interventions to reduce reperfusion injury:

- Cyclosporine-A: inhibiting the opening of the MPTP.
- Metoprolol: contrary to the classical theory of reduced myocardial oxygen consumption, the mechanism responsible for this infarct-limiting effect is on circulating neutrophils and platelets) rather than cardiomyocytes.
- Glucagon like peptide-1 (GLP1) analogs: use of glucose to protect cardiomyocytes from energy depletion.
- ABCIXIMAB: Glycoprotein IIb/IIIa inhibitors were developed for the reduction of thrombotic events due to their potent effect on platelets and platelet leukocyte aggregates implicated in reperfusion injury (Ibáñez, 2015).

## Conclusion

The “lethal reperfusion injury”, is currently accepted to significantly contribute to the final infarct size, and of late has become the topic of intensive research. There has been an increasing interest from basic and clinical researchers in identifying novel therapeutic strategies to attenuate lethal reperfusion injury and opportunities to translate these strategies into improved patient care (Duicu, 2013).

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