10th ANNUAL SUMMER MENTORSHIP IN
REPRODUCTIVE MEDICINE
JUNE 26th – JULY 28th, 2017

AMERICAN CENTER FOR REPRODUCTIVE MEDICINE

CLEVELAND CLINIC

SYNOPSIS
OF
SCIENTIFIC WRITING PROJECT
1. Oxidative stress in male infertility – Alleviation and treatment

Background:
Numerous studies suggest that oxidative stress (OS) is a major cause of bodily dysfunction, disease, aging and others including male infertility. Globally, an estimate of 15 to 20 million couples are at reproductive age are infertile, of which about 40% to 50% have to attributed to male factor infertility, which is with a prevalence of about 7% even higher than that for a so-called common disease, diabetes mellitus. In about 40% of these infertile men oxidative stress has been identified as a major factor and can be caused by male genital tract infections, inflammations, varicocele, testicular heat stress, smoking, malnutrition, exposure to environmental toxicants or obesity, among others.

OS is an imbalance between oxidants and reductants or antioxidants in the body whereby the oxidants are extremely reactive compounds, mostly having single, free, unpaired electrons in the molecule. Such molecules are called radicals. Since most of these highly reactive compounds are derivatives of oxygen, these molecules are called reactive oxygen species (ROS). Equivalent, but less reactive nitrogen derivatives are reactive nitrogen species (RNS). Hydrogen peroxide (H$_2$O$_2$), although not being a radical, is also called among these ROS as it is also very reactive. This molecule can penetrate plasma membranes just like water and therefore cause damage inside cells. On the other hand, the reductants (antioxidants) are molecules that can donate electrons thereby “detoxifying” the oxidants. Molecules and substances in this group are vitamins, glutathione, lycopene, ubiquinol or enzymes such as catalase or superoxide dismutase. In the broadest sense, one can also count certain trace elements such as zinc or manganese in this group as they significantly contribute to the activation of antioxidative enzymes.

Considering that spermatozoa have an extraordinary high amount of polyunsaturated fatty acids in their plasma membrane, which is essential for their function, male germ cells are extremely susceptible to oxidation. On the other hand, a small amount of ROS is essential to trigger physiological functions of...
spermatozoa such as capacitation without which the man would also be infertile. Therefore, under normal conditions, the body maintains a very fine balance between oxidants and antioxidants. If this balance, though disease or unhealthy lifestyle, is thrown out of balance into the direction of an overwhelming amount of oxidants, we are talking about oxidative stress.

With regard to male infertility, clinicians need to analyze this imbalance and find the cause thereof. Conditions like infections/inflammations or varicocele can relatively easily be diagnosed and treated accordingly. However, for other causes of OS this is more difficult, mainly because of difficult diagnostic procedures or simply because scientists still do not know where this said balance is laying. As a result, patients are taking prescribed antioxidants. Often, however, patients are also taking over-the-counter antioxidants because they are allegedly healthy. This results in an unhealthy high concentration of antioxidants in the body causing so-called reductive stress, which is as dangerous as OS as it can cause dysregulations, heart or neurological diseases or infertility.

**Significance:**
In this review we will discuss causes of oxidative stress and its possible alleviation and treatment to improve male fertility.

**Outline:**
1. What is oxidative stress?
2. What causes oxidative stress?
3. Physiological ROS
4. Non-physiological ROS
5. Treatment of conditions generating OS
6. Antioxidative treatments
7. Effectiveness of antioxidative treatments
8. Reductive stress
9. Healthy diet and sperm DNA fragmentation
Synopsis of Writing Project

**Literature review:**

Preliminary literature search has been done. An exhaustive literature review needs to be done before the article.

**Journal:**

To be decided.

**Suggested reading:**

**Resources**

2. Opuwari CS, Henkel RR (2016); An update on oxidative damage to spermatozoa and oocytes. Biomed Res Int 2016: 9540142
5. Agarwal A, Majzoub A (2016); Role of antioxidants in male infertility. BJUI Knowledge, 1-9
9. Naviaux RK (2012); Oxidative shielding or oxidative stress? J Pharmacol Exp Ther 342: 608-618

**Intended audience:**

Urologists, Andrologists, Male infertility specialists

**Deadline:**

July 21, 2017