

**INTERNATIONAL JOURNAL OF NURSING DIDACTICS****RESEARCH PAPER****Developments in the Fight against Cancer Cachexia**

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**Cachexia** is a wasting syndrome in which both fat and muscle are lost due to the presence of tumor or inflammation. It implies a state of profound nutritional deficiency. This word is derived from the **Greek words kakos meaning bad, and hexis meaning condition**. This term is most often used to describe patients with chronic or end stage diseases such as cancer, AIDS, or cystic fibrosis. Affected patients lose weight and appetite and as a result become weak and fatigued. Drastic losses of body mass may lead to alterations in metabolic functions such as electrolyte balance. Electrolyte imbalances reduce strength, increase fatigue and weakness, and can cause numbness, tingling, involuntary twitching, and even pain. Severely malnourished individuals have difficulties performing even basic tasks such as bathing and grooming. In severe cases, starvation can result in death. Death is most likely a result of severe electrolyte imbalances that lead to arrhythmias. Death has also been reported due to weakened respiratory muscles leading to pneumonias that spread to the blood stream and result in fatal infection. Unfortunately, in cancer, Cachexia is present all too often.

Cachexia is really one of the most devastating symptoms of cancer – up to 75% of cancer patients suffer from this condition. It robs patients of their energy, quality of life, enjoyment, and ultimately sense of independence. Most patients afflicted with cancer Cachexia are those with cancers of the upper gastrointestinal tract. These include cancers of the esophagus, stomach, and pancreas. One study noted that 85% of all patients with pancreatic cancer develop Cachexia and lose a median of 14.2% of their pre-cancer weight just by the time of diagnosis. Average survival for patients diagnosed with pancreatic cancer is only nine to twelve months.

Cachexia is also seen frequently in lung cancer but is rare in patients with breast cancer, for example. Specifically, cancer related Cachexia does not usually occur in early stage cancer. It is seen almost exclusively with advanced and metastatic disease.

**WHAT ARE THE SIGNS AND SYMPTOMS OF CACHEXIA?:**

The foremost sign of Cachexia is drastic (greater than 10% of total body weight) **weight loss**. (Skeletal muscle atrophy

is also a frequent physical finding). This includes loss of both fatty tissue and muscle mass. Commensurate with this weight loss is a profound loss of appetite. Patients complain that they have no desire to eat and **lack any sense of taste**. Severe **anorexia**, therefore, can result in **weakness, fatigue, electrolyte imbalance**, and a **depressed immune system**.

**WHAT IS RESPONSIBLE FOR THE DEVELOPMENT OF CACHEXIA?:**

For a long time, scientists believed that cancer would soak up all the incoming nutrients to fuel its own growth and thereby starve the rest of the body. This theory proved to be unlikely, however. Even small tumors, that comprise less than five percent of the patients weight, can cause Cachexia. Furthermore, Cachexia can be seen in cancer patients receiving excess calories intravenously.

Early experiments using mice and rats showed that one can create a cachectic state in healthy animals by transfusing them with large amounts of blood from an animal with cancer Cachexia. With cessation of transfusions, the healthy animal's Cachexia resolves. When cancer stricken animals were operated on and the tumor was surgically excised, the animal gained weight. Such animal work has made clear, that there must be certain blood circulating substances produced the tumor itself that are responsible for the Cachexia. Recent data proved these substances are cytokines, such as tumor necrosis factor alpha, interferon gamma, cachectin, interleukin 1 and interleukin 6. In fact, when these cytokines are injected into healthy animals, Cachexia may ensue.

Cytokines are a class of substances that can affect the immune response. They are molecular mediators who may be thought of as the hormones of the immune system. It is not known exactly how cytokines are produced. Scientists believe that they can be produced the cells of the immune system or the tumor itself.

**WHAT HAPPENS TO A CACHECTIC INDIVIDUAL?:**

Lack of nutrition deprives individual cells of the carbohydrates, fatty acids, and amino acids, the building blocks for complex sugars, fats and proteins, respectively, that cells need to survive. The body senses this deficiency and begins to degrade healthy tissue for sources of energy. The degradation of healthy tissue is responsible for loss of lean body and muscle mass. Often, the body's consumption

of energy is also increased. In other words, the body's metabolic rate, even at rest, is significantly higher. Exactly how these metabolic changes occur is not completely understood. These changes are thought to be responsible for the patient's inability to gain weight even when caloric intake seems to be adequate.

Drastic weight loss is an independent risk factor for poor survival. Cachectic patients have worse outcomes with surgery, chemotherapy and radiation therapy. Cachexia is also an under recognized cause for distress and anxiety among patients and their family members as changes in body image are readily noticeable by everyone.

#### **TREATMENT FOR CACHEXIA:**

A number of therapeutic agents for cancer Cachexia have been investigated in the recent past. However, most studies are limited to a single tumor type and may or may not be applicable to all patients suffering from this condition. One of the biggest challenges in the treatment of Cachexia is the concern that extra calories would only "feed" the tumor rather than the starving healthy cells. For this reason any potential therapy must act through mechanisms that do not support tumor growth and spread.

One commonly used agent is essentially a hormone called megestrol acetate (Megace). This compound is a synthetic progestin hormone which works by interfering with the normal estrogen cycle thereby decreasing hormone levels overall. One of its side effects is appetite stimulation and weight gain. Its application in Cachexia came from this observed side effect when the drug was first used to treat hormone responsive breast cancer. Unfortunately, the weight gain is usually temporary and comes primarily as fatty tissue, rather than protein and muscle mass. All the same, maintaining weight and appetite are still important as they improve a patient's sense of wellbeing and may serve to increase activity level.

Some patients have been placed on corticosteroids in an attempt to increase weight. However, as with progestin, weight gain tends to be temporary and after a number of weeks, its use becomes counterproductive. With prolonged use, steroids interfere with muscle synthesis. It is unclear why these agents should work in the first place. One theory is that steroids interfere with cytokine production and action.

There is much research and recent press on the benefits of fish oils, especially ones that contains long-chain omega-3 fatty acids. A number of studies showed that fish oil supplements can stabilize weight loss and even increase weight in people suffering from cancer Cachexia due to

pancreatic cancer. One study in particular was able to show that omega-3 fatty acids can reduce inflammation and protein breakdown.

A drug called Thalidomide was initially marketed as a sleeping assisting medication. It was pulled off the market in the early 1960 when it was proven to be responsible for multiple birth defects when used by pregnant women. Now this drug may be used with caution to help people with Cachexia. The presumed mechanism of action appears to be cytokine interference.

Other possibilities currently under study include the statin family of anti-cholesterol medications and angiotensin-converting enzyme inhibitors that are used most often for hypertension. These medications are thought to have an anti-inflammatory component that maybe beneficial in suppressing cytokine production. A class of antibiotics known as the macrolides, which include, agents like Erythromycin and Azithromycin, has also been touted to possess anti-inflammatory properties. Creatin is a commonly used dietary supplement by athletes presumed to increase muscle strength and size. Its safety and efficacy is under study in cancer patients currently. Other supplements under consideration include amino acid supplements like cysteine which work toward increasing lean body mass.

The most drastic treatment for Cachexia, and one which is reserved as a last resort, is parenteral nutrition. Providing nutrients intravenously is both dangerous and expensive and is used only in desperate situations on a temporary basis. For short periods of time it can improve a patients' protein and electrolyte balance and assist a patient through a difficult course of therapy. For prolonged periods, the risk of life threatening infections outweighs the benefits.

#### **THE BIG PICTURE:**

As more is learned about Cachexia, it is now clear that it is not due exclusively to a caloric intake deficiency. Nor is it a consequence of tumor competing with healthy cells for the available nutrients. It is rather a complex metabolic change within the body. The metabolic changes are due to the presence of a malignancy and the inflammatory cytokines that it is thought to produce. The new knowledge in the mechanisms of Cachexia will lead to improved treatments, which will translate to improved quality of life.

Some scientists believe the next generation of Cachexia research and treatment will focus on inhibitors of protein degradation and stimulants of protein synthesis. Ideally, of course, improvements in anti-cancer therapy may make anti-Cachexia treatment obsolete.