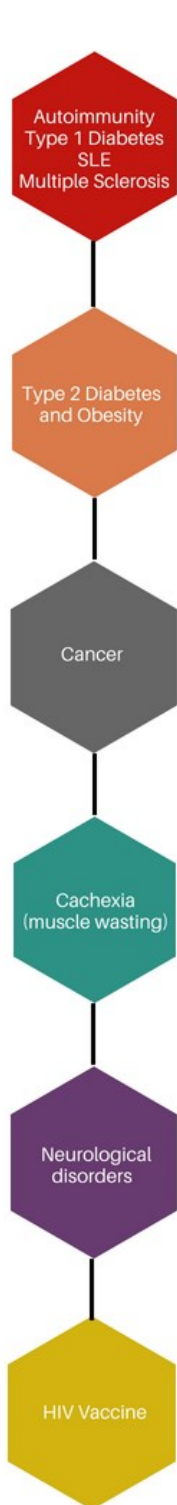


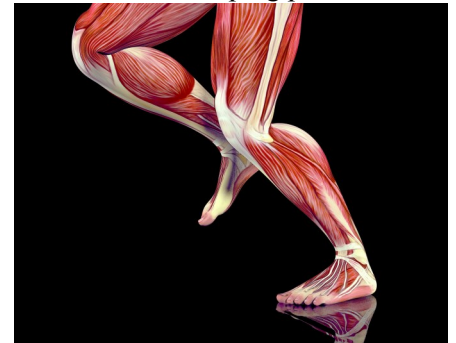
# The Bench and Beyond



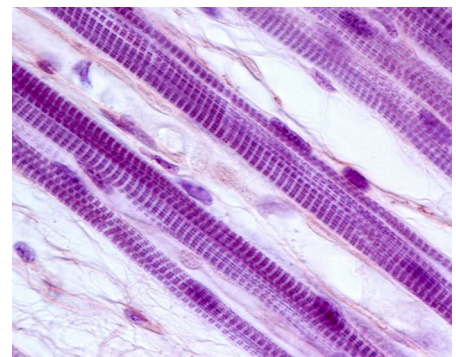
**Cachexia**, pronounced kuh-kek-see-uh, is the profound loss of muscle that is often seen in people with chronic conditions such as cancer, chronic infection, pulmonary disease, diabetes and heart failure. Cachexia is different from other types of weight loss in that it cannot be stopped or reversed by eating more food. Cachexia is a syndrome, not a disease, because it is characterized by a collection of symptoms that occur together. These symptoms are weight loss, muscle loss, loss of appetite, fatigue and diminished quality of life. It is incredibly debilitating, and is associated with poor response to medications and poor prognosis. Our understanding of cachexia has increased substantially over the past decade. We know that people with cachexia have an imbalanced immune system, and that their metabolic and inflammatory pathways do not function correctly.

We also know that these changes can promote and exacerbate cachexia. Despite all of this new knowledge, we cannot stop the process once it has begun, and there is no cure.

**What is happening in the muscle during cachexia?** Healthy muscle is very active and works hard to maintaining its size and strength. As part of the normal muscle housekeeping process, muscle proteins are broken down (a process called **protein degradation**) and replaced by new proteins (**protein synthesis**). In addition, parts of muscle cells that are no longer needed or that no longer work properly are eaten by the cell itself by a process called autophagy, and then replaced, and new muscle tissue develops by regeneration. During cachexia all of these processes stop working correctly. There is more protein degradation, less protein synthesis, more autophagy and less regeneration causing the destruction of muscle tissue.



**Cachexia research at SDBRI:** So far, no single drug has successfully reversed or stopped cachexia. This might be because a successful treatment would need to both stop all of the processes that cause muscle destruction, and promote muscle growth and there might not be a drug that can do that. The goal of the Davies research group is to identify the problems that cause cachexia at a very early stage, before cachexia begins. The idea is that if those changes can be corrected early, patients will not become cachexic in the first place. Over the past two years the Davies research group has identified several immune cell types in the blood of cancer patients that are present at higher levels in patients with stronger and larger muscles than in patients with smaller and weaker muscles. Ongoing research is aimed at understanding whether these immune cells can be used as markers to predict which patients will become cachexic and whether increasing the number of these cells might prevent the onset of cachexia in those patients.



*(The photo shows a section through skeletal muscle)*

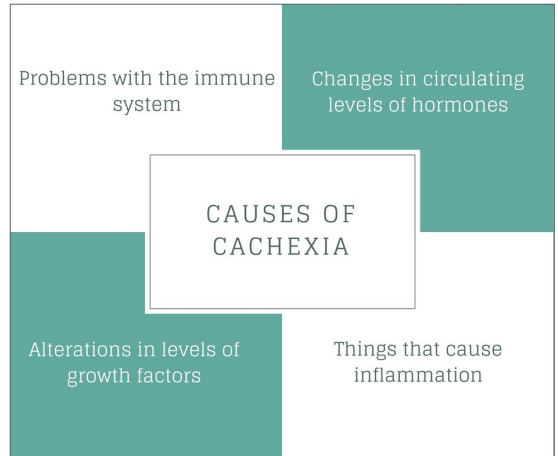
# Frequently Asked Questions!

**Is cachexia the cause of all types of severe muscle wasting?** No, there are other ways a person can lose muscle. A type of muscle wasting that is very similar to cachexia is sarcopenia. Sarcopenia is dominated by muscle wasting, loss of muscle strength, and poor quality of life. It is different from cachexia at the molecular level and is not associated with an underlying chronic disease. A reduction in physical activity, particularly in the elderly, increases the risk of sarcopenia.

**Does exercise and muscle training reverse cachexia?** It is not possible to stop or reverse cachexia through muscle strengthening training and exercise.

**What is the difference between someone who is thin and someone who is cachexic?** Cachexia is unintentional weight loss that cannot be corrected through diet. It is a process that actively reduces body weight and the size of muscle. It is not simply the act of being thin.

**What causes cachexia?** People with cachexia often have an array of health issues inside the body that are not obvious to the outside. These health issues range from problems with the immune system, changes in circulating levels of hormones, growth factors, and things that cause inflammation. All of these things can contribute to cause muscle wasting if too high or too low. It is not known how combinations of all of these things work together to cause cachexia, but it is clear that muscle is the target of multiple attackers.



**How is cachexia treated?** Cachexia is a multifactorial syndrome so it is best treated using several treatment strategies at the same time. Leaders in the field advocate for using therapies that target multiple biological pathways combined with exercise, and appetite stimulants. We believe that if we gain a better understanding of the molecular and cellular pathways that lead to cachexia, we should be able to identify markers that can predict it and design drugs that can prevent it. For those people who are already cachexic a successful treatment strategy will need to stop those processes that cause muscle destruction and simultaneously promote muscle health and strength.



## Next Issue:


Taking a closer look at Systemic Lupus Erythematosus


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