

Meal Spacing and Intermittent Fasting

By Dr. Ritamarie Loscalzo

It's quite common for people with blood sugar imbalances and/or excess weight to be told to eat frequent, small meals throughout the day. The idea is that eating every couple of hours keeps your blood sugar level steady and prevents the severe hunger that accompanies dips in blood glucose. In theory, when you eat frequent small meals, you never overeat.

Studying the biochemistry and recent hormone research has lead me to conclude that, for most people, this is actually the worst way to eat for blood sugar balance and weight loss and can actually be damaging to your health.

Understanding Why Frequent Eating is Faulty Advice

Hunger, satiation, and blood sugar balance are all under the hormonal control of what I like to call "the survival hormones."

Eating between meals alters powerful hormonal signals, interferes with the mechanism that burns fat as fuel, clogs liver metabolism, and sends calories right to fat stores.

Insulin is a hormone secreted by your pancreas in response to eating. It doesn't much matter what you eat; insulin will be secreted. The composition of your meal determines just how much insulin is secreted. The more carbohydrates in the meal, the more insulin that's required to keep your blood sugar regulated.

The most basic concept that you need to understand is that whenever insulin levels rise, fat burning stops.



The Hormone Relationship Between Insulin and Fat Burning

In order to understand why an increase in insulin affects your fat burning ability, let's start by understanding what should happen with hormones in a perfectly balanced body.

1. You eat, insulin levels rise, and glucose is moved into your cells to be burned for energy.
2. Insulin triggers leptin levels to rise (leptin is the hormone your fat cells secrete after a meal) which signals the brain to turn off your appetite and tells your pancreas to stop making insulin.
3. Growth hormone is released. Growth hormone, in the early post meal stages, triggers the build up of muscle protein, which is enhanced by the presence of insulin.
4. About three hours later, glucose levels return to normal and insulin should be back down to where it was before your meal.
5. Your liver begins to kick into high gear, mobilizing glycogen into blood sugar.
6. You begin to burn fats that are in your blood for energy, thus putting to good use fats that would otherwise go into storage, as unwanted fat!
7. More than four hours after eating, growth hormone begins to mobilize fat for fuel. However, this only happens when insulin levels are very low.
8. If your blood sugar begins to drop too much, glucagon is secreted to mobilize stored calories and all is well until your next meal.

Typically, insulin levels peak at around 30 minutes after you eat and return to normal at about 3 hours. Then leptin gets to go to work and triggers fat burning.

In the ideal situation, insulin sends 60% of the fuel in a meal to the liver for “quick access” storage as glycogen and triggers the uptake of the remaining 40% of the glucose and amino acids into muscle cells and cells of your vital organs, which use the glucose for fuel and the amino acids for growth and repair.

However, if you're eating every 2 – 3 hours, as some experts advise, your insulin levels never go back to normal and you never go into fat burning mode.



Eating small, frequent meals has never been proven to accelerate weight loss despite what many experts claim. In fact, there are many more studies that suggest that less frequent eating promotes more rapid weight reduction.

The period in between meals should be an opportunity for your liver to exercise and clear out glycogen. If you snack between meals or eat a meal too soon after the previous one, your liver's exercise routine is blocked, thus setting you up for obesity, insulin resistance, and diabetes. When your liver doesn't get enough exercise, it can synthesize excessive cholesterol, leading to elevated blood lipids even if the food you eat contains no cholesterol.

If your muscles are well toned, they will use up fat between meals much faster than untrained muscles. In fact, muscle tone can provide you with the energy that you need to keep going all day long.

When you eat too soon after a previous meal, insulin levels rise too soon, turning off your liver's exercise routine, inhibiting fat burning, and causing calories to be stored rather than burned. Plus, your energy will plummet and you may suffer from food cravings.

If you consistently eat meals too close together, you'll cause your pancreas to fatigue, your insulin receptors to become resistant, and you'll struggle with your weight.

Feeling weak or hungry sooner than 5-6 hours after eating a meal can be due to:

- Not eating enough at the previous meal
- Eating too many carbohydrates at the previous meal
- Impaired digestion and absorption
- Being out of shape
- Weak adrenals
- A sluggish and congested liver
- Exhaustion
- Diabetes
- Insulin resistance
- Leptin resistance



Understanding the Process of Becoming Insulin Resistant

When you eat frequent, small meals throughout the day, insulin levels stay elevated all day, triggering fat storage and leading to insulin resistance. What this means is that your cells no longer hear the cry of insulin to allow fuel in for energy. As result, more fat storage occurs and you feel tired all the time.

If everything is functioning properly, then after a meal there is no need to eat again for 5 or 6 hours.

The hormone **glucagon** is in charge of keeping your blood sugar steady between meals. Glucagon signals the liver to turn the stored glycogen back into glucose as your sugar levels begin to drop between meals. It also triggers a process called “gluconeogenesis” which triggers the creation of glucose from stored protein and fat.

In a healthy person, insulin and glucagon are good siblings and take turns.

There are enough carbohydrates stored in your liver in the form of glycogen to last 24 hours, unless you are engaging in extreme exercise like marathons or triathlons, so when things are functioning well, there are no blood sugar dips between meals.

Snacking between meals causes insulin to rise again (before it's returned to normal), suppresses glucagon, and raises leptin levels unnaturally -- leading to a condition called **leptin resistance** wherein the brain and pancreas no longer hear the signal from leptin to turn off appetite and reduce insulin secretion.

Constantly elevated levels of insulin from snacking between meals, deliberately planning meals close together, or eating foods high in sugar and simple carbohydrates, causes **hyperinsulinemia**, a condition of too much insulin in your blood. This condition leads to insulin resistance as the cells can no longer take in so much sugar and “close their ears” to the insulin signal.

Insulin resistance leads to weight gain, especially around the middle, stiffening of your arteries, elevated blood pressure, systemic inflammation, and eventually to cardiovascular disease like heart attack and stroke.



The Dangers of Insulin Resistance

Once you understand how the hormones are supposed to work together, you can understand why eating frequent, small meals is not just a bad idea for weight loss, it's outright dangerous.

In addition, eating too frequently can cause your liver to get congested. Remember, ideally, the liver takes 60% of the fuel from each meal and stores it as readily available fuel. When your liver becomes insulin resistant, those calories eaten head directly for fat storage as your liver can no longer accept them without the aid of insulin. Further, eating too often clogs your liver's fuel storage system, resulting in fatigue and impaired detoxification mechanisms.

Eating too often also triggers your liver to produce excess **VLDL**, the most dangerous form of cholesterol. As a result, snacking between meals causes cholesterol to rise, even more than eating cholesterol rich foods.

A Chain of Collapse

This whole process, a guaranteed “chain that makes you gain,” becomes a vicious, vitality-sabotaging cycle:

1. When your liver gets clogged and develops insulin resistance, it's hard to go 5-6 hours between meals or to sleep through the night because your liver can no longer produce a steady stream of glucose – it needs to come from outside.
2. When there is insulin resistance in your liver, your liver turns calories into fat at an increased rate, leading to excess weight.
3. The constant high levels of insulin due to eating too frequently result in excess leptin and eventually leptin resistance, which further confuses your liver and turns down the production of glucagon, the hormone that keeps your blood sugar steady between meals by stimulating the release of stored fuel.
4. To make matters even worse, the lining of your blood vessels and your nerve cells do not become insulin resistant and are subject to the stiffening effect of excess blood sugar and insulin.
5. The net result is stiffening of your arteries and hardening of your nerves, leading to cardiovascular disease and mental decline.



Breaking the “Gain Chain”: Solutions to Restore Your Hormones

As you can see, the biochemistry supports eating meals more frequently rather than less frequently. The ideal gap appears to be 5-6 hours between meals with a 12-hour period between dinner and breakfast.

According to Dr. Dennis Clark, author of *The Belly Fat Book*, “The recommendation of eating six small meals per day, to keep the furnace burning hot, has become dogma in some circles. However, the common advice for frequent meals to keep the body's furnace burning hot makes no sense physiologically or biochemically.”

Dr. Tim Crowe notes that some research suggests that playing around with when you eat may actually cause you to put weight on. “If feeding time determines the activity of a large number of genes completely independent of the circadian clock, when you eat and fast each day will have a huge impact on your metabolism,” says the study's leader, Satchidananda (Satchin) Panda, Ph.D., an assistant professor in the Regulatory Biology Laboratory.

Panda points out that the activity of fat-burning genes is highest when you haven't eaten for a while. Thus, extending time between meals and not eating after dinner actually turns on liver genes that enhance your ability to lose weight or maintain a healthy weight.

The three meals per day eating pattern becomes more critical for keeping a low body fat percentage as you age, as metabolism slows down. This can be partly corrected by regular strenuous exercise.

If you think you can't space your meals because you have hypoglycemia, think again. Most people who claim they are hypoglycemic (and attribute feeling uncomfortable if they skip meals) really don't experience true hypoglycemia. Many of the people I've worked with have discovered that their blood sugar is actually up when they experience the out of balance feelings they were misled into believing were symptoms of low blood sugar.

Get a blood glucose meter and check your blood sugar between meals.



Many people do experience what's known as "reactive hypoglycemia," where their blood sugar plummets after being high (triggering too much insulin secretion), then going too low because of the over-clearance of sugar from the blood due to high levels of insulin.

When hunger comes on too soon, stave it off with water flavored with essential oils or lemonade made with water, lemons, and a pinch of stevia if desired.

Make friends with hunger. It can be your friend. Hunger indicates that your body is in fat burning mode. The hormone **ghrelin**, secreted by your stomach, triggers hunger but also triggers the release of **growth hormone**, your fat burning friend.

If you learn to tolerate a little hunger and gradually increase the space between meals, you'll be rewarded by weight reduction, hormone balance and improved blood lipids. So, now that you understand the dangers of eating frequent, small meals and how they affect your hormone balance, what's the solution?

Timing Your Meals to Optimize Hormones is Essential

It's important to remember that fat burning is impossible when insulin levels are elevated. It takes about 3 hours after a meal for insulin levels to return to baseline, even if you just eat a small snack.

Until then, fat burning is impossible.

If you have weight to drop, are fatigued, concerned about family history of heart disease, cancer or diabetes, make use of that critical fat burning time.

At 3 hours after a meal, do some exercise, drink some water with lemon juice. and do whatever it takes to hold off the next meal for as long as you comfortably can.

It may only be 3 hours and 15 minutes to start, then 3 hours and 30 minutes, and then eventually, in 15 – 30 minute increments, you'll be able to gradually move your meal spacing to at least 5 – 6 hours.



Many children, young adults, bodybuilders, athletes, and fitness trainers can, without apparent consequences, violate the meal spacing required for optimizing fat burning. This is because their demand for calories to aid growth and body repair is very high.

Appropriate meal spacing becomes more important for people after the age of 30 or after intense training stops. In such cases, continued frequent eating will cause a gradual increase in percent body fat. It may show up either as added weight or as loss of muscle in proportion to fat.

As you stretch the time between meals and change the foods you eat to foods that require less insulin, you'll see the pounds melt away, your energy rise, and your mental clarity improve. And maybe, even more importantly, you'll protect yourself from the top 3 killer diseases in our modern world.

Meal frequency has been a topic of research for more than 40 years. Even though modern authors are recommending eating more frequently in spite of the biochemical evidence that fewer meals are more advantageous, there are no studies to support more frequent meals.

In *Eat Stop Eat*, Brad Pilon quotes Dr. Tim Crowe, a nutrition specialist at Deakin University in Melbourne, as saying the six-meal-per-day diet is a "faddish dieting trend," with very little research in support of it.

Intermittent Fasting for Fat Loss and Reduction of Insulin Resistance

The Sweet Spot Solution diet is designed to aid in the repair and re-sensitization of insulin receptors. Healing can only happen when insulin levels are low. Fat burning also happens only when insulin is low.

So what if we took this to the extreme and eliminated all food for a period of time? How would that affect your weight and insulin resistance? What about energy, strength and endurance?

Fasting means not eating at all. You already do this multiple times every day between meals. Breakfast means breaking your overnight fast between dinner and your morning meal the next day.



Well it turns out that short fasts actually accelerate fat burning and reverse insulin resistance. One of our members, diabetic for many years and on medication, did just that.

After 2 short fasts, she got off her medication and dropped her fasting from low 200's to low to mid 100's. As a result of continuing the healing on *The Sweet Spot Solution*, her blood sugar continues to drop. She reported that her fasting glucose readings are now in the 80's.

Even though fasting has been thought to decrease metabolic rate and waste lean muscle mass, the studies say otherwise and support the overall benefits of fasting to your long term health.

In addition, it turns out that endurance athletes actually burn more body fat while fasting than when fed, according to a study the *European Journal of Applied Physiology and Occupational Physiology* published in 1987.

While the downside of long-term fasts is a slower metabolism and the breakdown of lean muscle tissue, short fasts of 24 – 72 hours actually may increase fat burning and metabolic rate. Short fasts can also slow down aging, build muscle mass, tone your skin, and even reverse some chronic health problems. A one day per week fast has been shown to boost your fat metabolism by optimizing the critical hormones involved in storing and using fat.

Fasting is the simplest method your body has for maintaining caloric balance. Healing and repair, as well as fat burning, happens during the fasting state. Unfortunately, many people spend 16 or more hours a day in the fed state.

I'm sure you've heard that if you lower your calorie intake too much, even for a short period of time, you'll stop losing fat because your body goes into 'starvation mode' and your metabolic rate slows to a standstill.

Short Fasting and the Myth of Going Into “Starvation Mode”

This statement is not supported by modern research or ancient wisdom. Here's just a sampling of research studies that show increased fat burning during fasting, with no impact on metabolic rate, endurance, or strength.



In a study conducted at the University of Nottingham (Nottingham, England), researchers found that when they made 29 men and women fast for 3 days, their metabolic rate did not change. So much for needing to eat every three hours!

A study at the Pennington Biomedical Research Center found that men and women who fasted every other day for a period of 22 days experienced no decrease in their resting metabolic rate.

Another study published in the *Journal of the American College of Nutrition* found that the resting metabolic rate of people who were on a diet of 800 calories a day for 12 weeks AND completed resistance exercise did not change. Apparently fasting and low calorie diets don't cause the loss of muscle mass if you are doing resistance training.

Obesity Research published a study that found that women who ate half the amount of food that they normally eat for three days in a row saw no change in their metabolism, either.

The *British Nutrition Journal* published studies that found no change in the metabolic rate of men and women between the ages of 25 and 65 who skipped breakfast, or people who ate two meals a day compared to seven meals per day.

Based on these and hundreds of other studies that have been performed on metabolic rate, calorie restriction, and fasting, it appears that your metabolism is much more closely tied to your **lean body mass** than anything else.

What's the best way to increase lean body mass and this increase metabolic rate?
Resistance exercise.



Fasting and Exercise

Short fasts or periods of caloric restriction do not seem to have an effect on muscle mass or strength as long as you are exercising.

Research published in the *European Journal of Applied Physiology and Occupational Physiology* found that a three-day fast has no negative effects on how strongly your muscles can contract, your ability to do short-term high intensity exercises, or your ability to exercise at moderate intensity for a long duration.

An interesting 2007 study in the *Journal of Physical Activity and Health*, 2007, compared performing 90 minutes of aerobic activity by people who had just completed an 18-hour fast to those who had recently eaten and to those who were supplementing with carbohydrates during their workouts. There was no difference.

Even soldiers who were exercised to exhaustion performed similarly whether they were well fed or had just fasted for three and a half days, according to a study in the *Journal of Applied Physiology*.

In his book *Eat Stop Eat*, Brad Pilon reported a study published in 1986 where nine men who were experienced long distance runners were asked to run at 70-75% of their V02 Max for 90 minutes twice, once while fed and the other at the end of a 23-hour fast, about 2 weeks later. When the blood glucose levels of the runner's first run and second run were compared, no difference was found. Plus, the fat burning rate of the fasting run was greater than the fed run.

Interestingly enough and very pertinent to you as a *Sweet Spot Solution* participant, it also took almost 30 minutes of exercise for the insulin levels of runners in the fed state to be the same as those who were fasting BEFORE they even started their run.

Fasting and exercising have a dramatic effect on maintaining blood glucose levels. Contrary to popular belief, fasting does not negatively impair mental alertness or high level thinking. In fact, those patients of mine who've fasted for 24 hours or longer report increased mental clarity.



In 2008, the *American Journal of Clinical Nutrition* published a study that found that university students performed equally well on a series of intellectual tests after having compared eating a normal meal, skipping one meal, skipping two meals, or going 24 hours without food.

A study published in the *European Journal of Applied Physiology* found that fasting can actually make you more sensitive to the anabolic effects of protein intake and exercise on muscle growth. Intermittent fasting may actually allow for better muscle growth.

Taking short breaks from eating allows you to retrain your relationship with food, get comfortable with having an empty stomach, notice when you are full, and subsequently eat less when you do eat.

Short-term fasting decreases leptin levels and can help restore the sensitivity of your hypothalamus and pancreas to the full signal of leptin. Fasting also increases growth hormone (GH) so that fat loss remains high during periods of fasting.

Halberg N, et al. published findings in the *Journal of Applied Physiology* showing that fasting for as little as 24-hours drastically reduces your insulin levels, thus allowing fat burning to be optimized, and helping to restore insulin sensitivity.

This was confirmed by research published in the *American Journal of Physiology* done on people who fasted for 72 hours. Plasma insulin levels dropped to less than half of its initial levels. 70% of this reduction happened during the first 24 hours.

Amazingly, a 24-hour fast can have a more dramatic impact on reducing insulin than low carbohydrate diets alone. If you want to bring your insulin levels down quickly, short-term fasting appears to be the most effective way. Intermittent fasting (fasting 1 or two days a week, for 24 hours) appears to be a very valuable strategy for reversing insulin resistance, burning fat, and improving the results of *The Sweet Spot Solution* program.

Fasting once or twice a week allows your insulin levels to become very low and alternate with periods of normal levels. This gives your insulin receptors a needed rest, allows your blood vessels to heal from the over exposure to insulin, and allows your blood sugar regulating system to return to balance much more rapidly.

If you are feeling stuck, intermittent fasting just may be the key to getting unstuck and making dramatic progress.



On top of the positive effects of short-term fasting on bringing insulin and blood glucose levels down, research has shown that short-term fasting can result in a six-fold increase in growth hormone.

Growth hormone also plays a big role in keeping your metabolism elevated. Eating and insulin secretion prevent the release of growth hormone. Therefore, metabolism, is positively affected by short-term fasting.

According to a study in the *Journal of Clinical Endocrinology and Metabolism*, growth hormone causes more fat loss in the fasted state than in the fed state; therefore, providing more evidence that intermittent fasting is a boon to insulin sensitivity and fat burning.

The journal *Aging Cell* in 2010 published a study that showed that fasting, not just caloric restriction, was needed to significantly increase growth hormone. The *Journal of Clinical Endocrinology Metabolism* confirms that exercise results in a greater increase of growth hormone than fasting alone.

Not surprisingly (once you understand the hormonal influence of short-term, intermittent fasting) is that people who use intermittent fasting as a weight loss method lose more weight in a 10-week period than people on a very low calorie diet and they maintain their weight loss longer.

Intermittent fasting can be used as a very effective way to maintain optimal insulin and blood glucose levels, in addition to an excellent weight maintenance strategy. If you fasted twice a week to reduce your weight, then perhaps fasting once a week will help you maintain it. It will also keep your insulin levels lower and growth hormone higher.



Intermittent Fasting Strategies:

According to Pilon, author of *Eat Stop Eat*, and others, fasting for 24 hours once or twice a week is the best way to let go of extra pounds, maintain muscle, and to reap the amazing health benefits associated with fasting, including better blood sugar control and cardiovascular health.

Try it out by fasting once a week for 24 hours. If you would like to accelerate your progress, do it twice a week. It's best if the 2 days are not consecutive.

Here are some options for a variety of short fast lengths:

- **Breakfast to breakfast:** Eat breakfast on day 1, skip lunch and dinner, and have breakfast an hour later on the second day (24 hours).
- **Lunch to lunch:** Eat lunch on day 1, then skip dinner and breakfast the next day. Eat lunch on day 2 an hour later than on day 1 (24 hours).
- **Dinner to dinner:** Eat an early dinner on day 1, then skip breakfast and lunch the next day. Eat dinner on day 2 an hour later than on day 1 (24 hours).
- **Breakfast to lunch (extended):** Eat breakfast on day 1, skip lunch and dinner, then skip breakfast the next day and eat at lunch on day 2 (approximately 31 hours).
- **Breakfast to dinner (extended):** Eat breakfast on day 1, skip lunch and dinner, skip breakfast and lunch on day 2 and eat at dinner on day 2 (about a 36-hour fast).

Experiments at *Salk Institute* revealed that the daily waxing and waning of thousands of genes in the liver, your body's metabolic factory, is mostly controlled by food intake and not by the body's circadian clock as conventional wisdom had it. Thus, you have the tools to modify your metabolism by what and when you eat.



Conclusion

Meal spacing is a controversial topic. The popular belief that eating small, frequent meals is best for maintaining blood sugar balance and optimal weight are not supported by the research or the biochemistry.

When you eat small frequent meals, your body is in a constant mode of elevated insulin. Under high insulin conditions, growth hormone is inhibited and fat burning is turned off. Frequent eating leads to leptin resistance, insulin resistance, and excess weight. Based on the biochemistry, the spacing between meals that works best is 5-6 hours.

Longer periods of time in the fasting state provide even more benefits including lower insulin and glucose levels, higher growth hormone levels, reduction of insulin resistance and leptin resistance, and increased metabolic rate.

Intermittent fasting is an extreme form of meal spacing. Fasting for 24 hours once or twice a week can accelerate your progress towards a lean, strong body, balanced blood sugar and vibrant health.

Give it a try and see if it's for you.



References

- Br J Nutr. 2010 Apr;103(8):1098-101. Epub 2009 Nov 30. Cameron JD, Cyr MJ, Doucet E *Increased meal frequency does not promote greater weight loss in subjects who were prescribed an 8-week equal calorie, energy-restricted diet.*
- Christopher Vollmers, Shubhroz Gill, Luciano Di Tacchio, Sandhya R. Pulivarthy, Hiep D. Le, and Satchidananda Panda *Time of feeding and the intrinsic circadian clock drive rhythms in hepatic gene expression* Proceedings of the National Academy of Sciences 2009 November Salk Institute for Biological Studies.
- Byron J Richards, CCN, *Mastering Leptin.*
- Byron J Richards, CCN, *The Leptin Diet: How Fit Is Your Fat.*
- Clark, Dr. Dennis. PhD. *Belly Fat Book: 5 Steps to a Slimmer and Healthier You.*
- Pilon, Brad, MS. *Eat, Stop, Eat.*
- Webber J, Macdonald IA. *The cardiovascular, metabolic and hormonal changes accompanying acute starvation in men and women.* British Journal of Nutrition. 1994; 71:437.
- Heilbronn LK, et al. *Alternate-day fasting in non-obese subjects: effects on body weight, body composition, and energy metabolism.* American Journal of Clinical Nutrition. 2005; 81:69-73.
- Bryner RW. *Effects of resistance training vs. Aerobic training combined with an 800 calorie liquid diet on lean body mass and resting metabolic rate.* Journal of the American College of Nutrition 1999; 18(1): 115-121.
- Keim NL, Horn WF. *Restrained eating behavior and the metabolic response to dietary energy restriction in women.* Obesity Research. 2004; 12:141-149.
- Verboeket-Van De Venne WPHG, et al. *Effect of the pattern of food intake on human energy metabolism.* British Journal of Nutrition. 1993; 70:103-115.
- Bellisle F, et al. *Meal Frequency and energy balance.* British Journal of Nutrition. 1997; 77: (Suppl. 1) s57-s70.
- Knapik JJ, Jones BH, Meredith C, Evans WJ. *Influence of a 3.5 day fast on physical performance.* European Journal of Applied Physiology and Occupational Physiology 1987;56(4):428-32.



- Schisler JA, Ianuzzo CD. *Running to maintain cardiovascular fitness is not limited by short-term fasting or enhanced by carbohydrate supplementation.* Journal of Physical Activity and Health. 2007 Jan;4(1):101-12.
- Knapik JJ, Meredith CN, Jones LS, Young VR, Evans WJ. *Influence of fasting on carbohydrate and fat metabolism during rest and exercise in men.* Journal of Applied Physiology 1998; 64(5): 1923-1929.
- Loffreda S, Yang SQ, Lin HZ, Karp CL, Brengman ML, Wang DJ, Klein AS, Bulkley GB, Bao C, Noble PW, Lane MD, Diehl AM. *Leptin regulates proinflammatory immune responses.* Federation of American Societies for Experimental Biology Journal. 1998 Jan;12(1):57-65.
- Esposito K, Nappo F, Marfella R, Giugliano G, Giugliano F, Ciotola M, Quagliaro L, Ceriello A, Giugliano D. *Inflammatory cytokine concentrations are acutely increased by hyperglycemia in humans: role of oxidative stress.* Circulation. 2002 Oct 15;106(16):2067-72.
- Dixit VD. *Adipose-immune interactions during obesity and caloric restriction: reciprocal mechanisms regulating immunity and health span.* Journal of Leukocyte Biology. 2008; 84:882-892.
- Morgan TE, Wong AM, and Finch CE. *Anti-inflammatory mechanisms of dietary restriction in slowing aging processes.* Interdisciplinary Topics in Gerontology. 2007; 35:83-97.
- Fontana L. *Neuroendocrine factors in the regulations of inflammation: Excessive adiposity and caloric restriction.* Experimental Gerontology. 2009; 44:41-45.
- Leiberman HR, Caruso CM, Niro PJ, Adam GE, Kellogg MD, Nindl B, Kramer FM. *A double blind, placebo-controlled test of 2 d of calorie deprivation: effects on cognition, activity, sleep, and interstitial glucose concentrations.* American Journal of Clinical Nutrition 2008;88:667–76.
- Deldicque L, De Bock K, Maris M, Ramaekers M, Nielens H, Francaux M, Hespel P. *Increased p70s6k phosphorylation during intake of a protein-carbohydrate drink following resistance exercise in the fasted state.* Eur J Appl Physiol. 2010 Mar;108(4):791-800.
- Halberg N, et al. *Effect of intermittent fasting and refeeding on insulin action in healthy men.* Journal of Applied Physiology 2005; 99:2128-2136.
- Hartman ML, et al. *Augmented growth hormone (GH) secretory burst frequency and amplitude mediate enhanced GH secretion during a two-day fast in normal men.* Journal of Clinical Endocrinology and Metabolism 1992; 74(4):757-765.



- Vendelbo MH, Jorgensen JO, Pedersen SB, Gormsen LC, Lund S, Schmitz O, Jessen N, and Moller N. *Exercise and fasting activate growth hormone-dependent myocellular signal transducer and Activator of transcription-5b phosphorylation and Insulin-like growth factor-1*. Moller L, Dalman L, Norrelund H, Billestrup N, Frystyk J, Moller N, and Jorgensen JOL.
- *Impact of fasting on growth hormone signaling and action in muscle and fat*. Journal of Clinical Endocrinology and Metabolism. 2009;4: 965-972.
- Redman LM, Veldhuis JD, Rood J, Smith SR, Williamson D, Ravussin E; Pennington CALERIE Team. *The effect of caloric restriction interventions on growth hormone secretion in non-obese men and women*. Aging Cell. 2010 Feb;9(1):32-9.