Effects of Long Fasting on Health

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Introduction

The issue of healthy eating has long been an important concern to individuals and cultures. Fasting is the practice of abstaining from food or water, for an extended period of time. It is an ancient practice undertaken for spiritual, health and political benefits. The practice of prolonged fasting for political or religious purposes is on increase (**Kerndt 1982**).

Fasting, along with other practices like dieting, and vegetarianism are techniques employed by individuals and encouraged by societies to increase longevity and health. Long-term calorie restriction (CR) causes many physiological changes that alter life-history traits such as growth, reproduction and lifespan. Studies have shown that reducing typical calorie consumption by 30-40% extends life span by a third or more in many animals, including nematodes, fruit flies and rodents (**Stripp 2013**). Contrary to popular belief, fasting isn't dangerous or unhealthy; it's actually healthy and beneficial if it's done properly.

Definition

As religious philosophy and customs evolve; the term fasting has become more liberal and loose in its application. This is evident from its definition found in Wikipedia, which reflects the blurry lines between fasting and dieting prevalent today.

Fasting is a willing abstinence or reduction from some or all food, drink, or both, for a period of time to focus on health and / or spiritual upliftment (**Wikipedia**). An absolute fast or dry fasting is normally defined as abstinence from all food and liquid for a defined period, usually a period of 24 hours, or a number of days. Water fasting allows drinking water but nothing else. Other fasts may be partially restrictive, limiting only particular foods or substances. A fast may also be intermittent in nature. Fasting practices may preclude intercourse and other activities as well as food

Apart from fasting and dieting, there is another phenomenon known as "starvation" which shares a few traits with fasting. However, starvation is the result of lack of food and drinks due to lack of access or means and not a desirable and voluntary act like fasting.

There is no standard duration for fast and it can range from twelve hours to three months or more. Depending on the duration of the fast, it is classified as "short" and "long" fasting. Short fasts have duration from 8 hours to three days and are undertaken more frequently. Prolonged fasts are undertaken from three days to typically one month, although longer durations have been recorded. The longest recorded fast was that of a 27-year-old

obese man who fasted 382 days and lost 125 kg with no major side effects (**Kerndt 1982**). Intermittent fasting (IF) involves fasting for shorter periods of time on a regular basis.

Depending on the role of water in the fast, it is classified as "dry" and "water" fasting. Dry fast is the most extreme form and requires that no food or water is consumed during the period of fast. Water fasting on the other hand includes drinking water, but no other liquid and calorie intake is included. There exist other techniques like juice fasting, fast on broth, or low-calorie protein fast. However, these are not considered true fast from spiritual and medical view. This article focuses on dry and water fasting: the benefits, the drawbacks, and precautions.

Table 1: Comparison between Dry/Water Fasting, Dieting and Starvation

	Food intake	Water Intake	Motivation
Dry Fasting	None	None	Spiritual, Health and Political benefits
Water Fasting	None	Normal	-do-
Dieting	Reduced	Normal	Health, Cosmetic benefits
Starvation	None	None	None

History

The history of fasting dates back to antiquity. Since early times, fasting has been advocated for spiritual development and promotion of health. Ancient traditions require that one should fast before undergoing an important event in their life. Fasting has been a part of human customs even before major religions were established and it was required in preparation for many rituals that sought contact with supernatural forces. Great importance was placed on fasting as a means of arousing ecstatic forces, dreams or visions. The belief on the spiritual benefits of fasting is prevalent in Christianity, Islam, Buddhism, Hinduism, Jainism and other religions. All 24 Jain Tirthankers have been cited for undertaking prolonged fasts and meditation to achieve salvation. Fasting is also mentioned in great religious books like the Jain Agams, Bible, Quran, Mahabharata, and Upanishads.

Not only humans, but even animals fast during times of stress or illness. It is a natural tendency for the organism, whether human or animal, to seek rest, balance and to conserve energy at critical times. Many of the great doctors of ancient times and many of the oldest healing systems have recommended it as an integral method of healing and prevention. Ayurvedic medicine, the world's oldest healing system, has long advocated fasting as a major treatment. Hippocrates, Plato, Socrates, Aristotle and Galen all praised the benefits of fasting.

The scientific study of the health benefits of fasting seriously began in 1935 when Clive McCay and his colleagues observed that restricting the calories fed to rats in a laboratory, without producing malnutrition, prolonged their lifespan (**McCay et al 1935**). Thus science of Calorie Restriction (CR) was born.

Physiology of fasting

While the spiritual importance of fasting is widely known, its physical effects on the body are less clear. Currently, the bulk of the scientific evidence for the health benefits of intermittent fasting has come from animal studies (**Longo and Mattson, 2014**). When the intake of food is temporarily stopped, many systems of the body are given a break from the hard work of digestion. The extra energy gives the body the chance to heal and restore itself, and burning stored calories gets rid of toxic substances stored in the body.

Metabolic adjustment

Metabolic changes with fasting are decreased body mass, increased high-density lipoprotein cholesterol (HDL or good cholesterol), decreased triglycerides and low-density lipoprotein cholesterol (LDL or bad cholesterol), lower fasting glucose and insulin concentrations, increased sensitivity to insulin-mediated glucose uptake and reduced biomarkers of oxidative stress and markers of inflammation (including CRP, IL-6, TNF, BDNF, and more) (**Horne 2008**).

Various changes in energy handling and calories during different phases of fasting are summarized in Table 2**.** In phase I of fasting (first couple of hours), the body fuel is glucose, largely from exogenous sources. From 4-16 hours (phase II**)**, the main source of glucose is hepatic glycogen (gluconeogenesis). Gluconeogenesis increases until the end of phase III. After phase III, glycogen stores are depleted and gluconeogenesis decreases significantly. This is where the body starts efficiently burning fat and ketones, while preserving muscle mass (**Kerndt 1982**). Subsequently, gluconeogenesis substrates come from muscle catabolism, recycled pyruvate and lactate, glycerol. During the first three phases of fasting, most people find difficult time to cope with, as metabolically these early phases of fasting are characterized by a high rate of gluconeogenesis with amino acids as the primary substrates. As the body's sugar levels drop and as the metabolism switches to the fat burning mode, ketone bodies comes to rescue and hunger comes down.

Table 2. Energy source during fasting

Duration of fast & Phase	(Phase I) 1-4 hours	(Phase II) 4-16 hours	(Phase III) 16-32 hours	(Phase IV) 32 hours-24 days	(Phase V) 24 days and on
Source of blood glucose	Exogenous	Glycogen Hepatic Gluconeogenesis	Hepatic Gluconeogenesis Glycogen	Hepatic & Renal Gluconeogenesis	Hepatic & Renal Gluconeogenesis
Major fuels of brain	Glucose	Glucose	Glucose	Glucose & Ketone bodies	Ketone bodies & Glucose

Glucose: Blood glucose levels fall early during fasting and remain low throughout the fasting period. There is appropriate reduction in insulin levels and increase in glucagon levels. Glucose homeostasis is essential because certain tissues, such as brain, erythrocytes, and cells of the renal medulla are obligate glucose users. While glucose levels are maintained by glycogenolysis, glycogen stores in liver rarely last more than 72 hours. During the early days of fast, there is a high rate of gluconeogenesis from non-carbohydrate sources, chiefly from amino acids, especially alanine, as substrates.

Fat: Fat in the form of triglycerides in adipose tissue provides the largest and most efficient storage of body energy. Fatty acid oxidation in liver cells generates ketone bodies that occur usually during the third day of a fast for men and the second day for women. As fasting continues, progressive ketosis develops and brain, muscles, and heart use ketones as a primary energy source. It is at this point in the fast that sensations of hunger generally go away. In addition, the hyperketonaemia exert a direct inhibitory effect on gluconeogenesis.

Protein: Protein, which has essential enzymatic, structural and mechanical functions, constitutes 15 percent of total body energy stores. As ketosis is not sufficient to meet energy requirement of the body, amino acids in muscle provide the balance. After prolonged fasts of more than a week, the body starts using non-body protein sources of fuel, such as degenerative tissues, bacteria, and viruses etc.

Protection of vital organs: The energy resources during the fast are mainly fat and to a lesser degree the cytoplasm of muscle, liver, bones marrow and other organ cells. A most brilliant design characteristic about life is that while we are fasting and securing our nutrition from many internal resources, not one minuscule fragment of the eyeball or the brain is consumed as food (**Khan et al 2011**). None of these living tissue structures are sacrificed. They are only reduced in size. The more vital the tissue, the less it is touched. The conservation of the body's protein is believed by many to be an evolutionary development

that exists to protect muscle tissue and vital organs from damage during periods of insufficient food availability.

Autophagy

This is the ability of the organism to selectively self-digest and removes unwanted material and accumulations from within the body without touching vital structures. In fasting, this quality is greatly enhanced so that many tumors, cysts, abscesses, abnormal accumulations, fatty deposits etc. may be completely or largely absorbed. Autophagy peaks when liver glycogen is depleted (around 12-16 hours of fast) then drops after about 2 days.

Electrolytes and minerals

Changes in trace metals and electrolytes are poorly defined. During the period of rapid weight loss, there is significant negative sodium balance, probably due to losses of the sodium salts of ketoacids in the urine. Concurrently there is depletion of potassium, phosphate, and magnesium (**Khan et al 2011**). There are variable responses in calcium and zinc levels during fasting. Homeostatic mechanisms maintain serum concentrations of these ions at the expense of intracellular stores. Thus serum levels may remain normal despite a marked reduction in total body levels. Potassium losses decrease after ten days of fasting. Magnesium calcium and phosphorous losses are minimal after the first week.

Pulse Rate & Blood Pressure

There is decrease in pulse rate and blood pressure during long fasting. Postural or orthostatic hypotension is due to the sodium losses plus a degree of autonomic insufficiency. Changes in electrocardiograms include sinus bradycardia, decreased QRS complex and T-wave amplitude, prolongation of the QT interval, and shifts to the right of the QRS and T-wave axes.

Hormonal changes

Glucose metabolism: There is a fall in insulin level and a rise in glucagon level.

Thyroid Hormone: The T4 level as well as TSH concentrations show slight decline from the early to the late fasting periods.

Growth Hormone: Human growth hormone shows an increase in later part of the fast. This rise is more marked in men than in women.

Gonadotropin: Serum luteinizing hormone and follicle-stimulating hormone levels fell during fasting and remained low after the first week of realimentation.

Role of the brain

Brain has a complex neural and humoral (chemical) circuitry to control food intake. Feeding is resumed either because of emptying of the digestive tract or because of fuel depletion by catabolism. Taste, and perhaps other (e.g. visual), receptors are stimulated by palatable food and motivation for feeding is increased. Signals from distended digestive tract and behaviour pattern results in satiety and feeding motivation is lowered. The net result of this interplay of positive and negative feedbacks from food responses is that body weight remains constant.

The neural circuitry involves limbic system and the hypothalamus that detect hunger and satiety signals from other parts of the body. The lateral hypothalamus has hunger centre that facilitates feeding responses. Electrical or chemical stimulation of this area elicits voracious feeding in satiated subjects and its destruction causes more or less prolonged noneating (aphagia). In contrast, the ventromedial (lower central) nucleus of the hypothalamus controls satiety. Subjects with lesions in this area stop feeding only at an abnormally high level of energy content and grossly overeat.

There are two peptides in the hypothalamus that produce hunger i.e. melanin concentrating hormone (MCH) and orexin. MCH plays a bigger role in producing hunger. Orexin plays a greater role in controlling the relationship between eating and sleeping. Other peptides in the hypothalamus that induce eating are neuropeptide Y (NPY) and agouti-related protein (AGRP). Satiety in the hypothalamus is stimulated by leptin. The arcuate nucleus also contains two more peptides i.e. cocaine- and amphetamine-regulated transcript (CART) and the second is α- melanocyte-stimulating hormone (α- MSH) that suppress hunger.

Molecular mechanism of benefits from fasting

Fasting acts in part as a form of mild stress that continually stimulates cellular defences against molecular damage (**Longo and Mattson 2014)**. It increases the levels of "chaperone proteins," which prevent the incorrect assembly of other molecules in the cell. Additionally, fasting mice have higher levels of brain-derived neurotrophic factor (BDNF), a protein that prevents stressed neurons from dying. In trying to find the mechanism by which CR produces its benefits, scientists have discovered a family of proteins called the *sirtuins* with a variety of functions in keeping cells healthy.

Psychological

Physical vs. psychological hunger: Fasting is not starvation but rather the body's burning of stored energy. It is estimated that even very thin people can survive for 40 days or more without food. When we experience hunger, it is not a true physiological (body) hunger, but rather psychological hunger. The sight and smell of food remain subjectively pleasant. Ketosis that develops during fasting, is commonly believed to be responsible for the anorexia.

When fast or calorie restriction is initiated, there is a critical transition period of about 3-6 weeks during which the body and brain adapt to the new eating schedule (**Longo and Mattson, 2014**). This period can be very uncomfortable, as restricted eating has been associated with extreme hunger, irritability, loss of strength, loss of libido, and other side effects (**Johnstone 2007; Heilbronn et al 2005**). Later on one may have false sense of well-being or euphoria. Once the body is accustomed, the hunger levels may decrease and mood could become more positive compared to before the fasting program started (**Kerndt 1982**).

Effect of Gender and Body Size

Lean persons become ketotic earlier than obese persons and women become ketotic more rapidly than men. However, gender differences disappear with increasing body weight. There is higher rise in glucagon, and growth hormone in obese persons compared to non-obese persons.

Benefits of fasting

Like all age-old customs and traditions, fasting has interesting health benefits that we are only discovering today with modern technology **(Wikipedia)**. Human organs regenerate during the fast. The possible benefits of prolonged fasting can be: detoxification, curing or alleviating acute and chronic illnesses and rejuvenation and/or attempts to increase life span. The benefits of prolonged fasting can be experienced after a person stops consuming food for more than 72 hours when they have depleted glycogen stores. The majority of health-specific findings related to fasting depends on breed of animal (human), age when fasting was initiated, health and disease status of individual, activity status including exercises, type and duration of fast, earlier food choices and eating habits (**Longo & Mattson 2014**).

Brain health

Mattson and other researchers (2004) have championed the idea that intermittent fasting (IF) lowers the risks of degenerative brain diseases such as Parkinson’s disease,

Alzheimer's disease and other neurological diseases. Fasting stimulates autophagy which results in removal of damaged molecules. They have also shown that periodic fasting protects neurons against various kinds of damaging stress, at least in rodents. In follow-up rodent studies, they also have observed that (IF) protects against stroke damage, suppresses motor deficits in a mouse and slows cognitive decline.

Mental Health

Though fasting may be religiously mandated, the social and communal traditions accompanying it are equally important. It brings families and social groups closer together. It often helps people suffering from depression and loneliness by reassuring them that they are not alone. Fasting is a way to "re-set" individual's relationship with food, break free from emotional eating and to start a fresh at the end of the fast.

Longevity

Even if calorie restriction (CR) does not help anyone live longer, a large portion of the data supports the idea that limiting food intake reduces the risks of diseases common in old age and lengthens the period of life spent in good health. Research in animals has shown that CR of up to 40 percent or fasting every other day (intermittent fasting) have an impressive positive effect on diseases, stress resistance, insulin sensitivity, markers of aging and life span (**Mattson et al 2004, Martin 2006**). Even though CR appears to work in a variety of species, its effects on longevity are not uniform. Although the links between CR and longevity are still not fully proven in humans, short-term human trials have clearly shown that CR can improve many vital surrogate health markers such as body weight, blood pressure, blood sugar, insulin, cholesterol and triglyceride levels and measures of inflammation.

Long Fasts and Weight loss

The most obvious and best-researched benefit of longer fasts is for weight loss. In fact long fasting is an effective way to lose weight quickly but with a danger of losing this gain once subject resumes old diet. Early in fasting, weight loss is rapid, averaging 0.9 kg per day during the first week and slowing to 0.3 kg per day by the third week. In the first three days, depletion of water is a major contributor to this quick weight loss. Other contributors are fat, glycogen and muscle tissue breakdown and the emptying of the colon. It is not certain whether intermittent fasting is better than continuous long fasting in preserving muscle tissues (**Johnstone 2007**). According to nutritionist, fasting should never be undertaken to lose weight and extended long fasting can lead to starvation.

Metabolic syndrome and atherosclerosis

One of fasting's main effects is to increase the body's responsiveness to insulin. Long-lived animals and people tend to have unusually low insulin (**Hatori et al 2012**). Decreased sensitivity to insulin often accompanies obesity and has been linked to diabetes and heart failure (**Mattson et al 2004**). There is a lowering of heart rate, blood pressure, atherosclerosis and risk for coronary disease (**Varady and Hellerstein 2007**). Findings of the Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy (CALERIE) pilot study in humans showed that overweight adults who cut their calorie consumption by 20 to 30 percent lowered their fasting insulin levels and core body temperature (**Stewart 2013**). Both of these changes correlate with increased longevity in animal models. The lower calorie intake also reduced their risk for major causes of mortality such as heart disease and diabetes (**Fontana et al 2004**).

Cancer

One of the amazing characteristic of fasting is the *autolysis or autophagy* as described earlier in this article. This can lead to digestion of tumor mass and improvement in malignancy. One of major side effect of cancer chemotherapy is immune system damage. Fasting helps, at least partially, in mitigating it by stimulating the regeneration of the immune system and shifting stem cells from a dormant state to a state of self-renewal. (**Cheng et al 2014).**

Other diseases

Calorie restriction and fasting delays the onset of many diseases such as autoimmune diseases, cardiomyopathies, renal diseases, neurodegenerative diseases and respiratory diseases. They can be used for most chronic condition including allergies, anxiety, arthritis, asthma, headaches and digestive disorders.

Long Fasts vs. Shorter Fasts

Studies have demonstrated that person doing long fast for physical and cosmetic reasons can have similar benefits from intermittent fasting (IF) also. IF also reduces many of the drawbacks of long fast. There’s typically no loss of lean tissue (muscle) with IF. There’s much less risk of malnutrition, heart failure, and infectious complications with intermittent fasting. Thus question arise weather long fasting is needed by them. On the whole, IF is superior for physical health (the same gain with less risk), but longer fasting may be superior for emotional, psychological, or spiritual reasons.

Restriction on Fasting

Restrictions have been imposed on too young (<15 years) and too old (>70 years); those suffering from illnesses (e.g. asthma, cancer, diabetes, eating disorders, schizophrenia, tuberculosis, ulcerative colitis etc.); women who are pregnant, lactating or menstruating; travelers who meet specific criteria; and individuals whose profession involves heavy labor and in whom fasting would be dangerous (**Longo and Mattson, 2014**).

Long Fasts: Dangers and Drawbacks

Although prolonged fasting is generally well tolerated with few and relatively minor complications, there are several reports of death occurring with it also. Medical supervision is recommended for any fast over three days particularly those with certain health conditions. Plenty of water should be taken by fasters since dehydration can occur. They should restrict their regular physical activity and exercise schedule.

Person doing long fast may experience side effects of fatigue, intense mood swings, malaise, aches and pains, emotional duress, irritability, anorexia nervosa, headaches, acne, allergies, swelling, vomiting, bad breath, and symptoms of colds and flu. Excessive intake of water without the corresponding amount of electrolytes can lead to hyponatraemia. Other complications seen in fasting include gout and urate nephrolithiasis more so in obese persons.

Cardiac: Fasting puts different types of stress on heart e.g. loss of cardiac muscle to energy demand and loss of minerals like magnesium and potassium. Person with pre-existing heart disease may have serious complications such as hypotension including postural hypotension, intractable ventricular dysrhythmias, and sudden death.

Infections: Worldwide, infectious diseases are the most common cause of death among starving people. In malnourished individuals particularly in children, immune system is weakened making them susceptible to infections.

Weight gain: Any fast longer than 48 hours runs the risk of metabolism to slow down and one may gain weight more easily once the fast is over (**Cheng 2014**).

Breaking a Fast

Introduction of feeding after a prolonged fast is an important issue. There is need to initiate refeeding gradually with instructions to eat small portions and more often. One must introduce easily digestible food such as soups, butter milk, well-cooked vegetables and cereals, and carbohydrate rich food.

Refeeding syndrome (RFS) is a well-recognized biochemical syndrome which occurs as a consequence of feeding after a period of starvation or fasting (**Khan et al 2011**). It was first reported in literature in 1950. In moderate to severe cases symptoms ranges from nausea, vomiting, and lethargy to respiratory insufficiency, cardiac failure, hypotension, arrhythmias, delirium, coma, and death. Hypophosphatemia and hypoalbuminemia are important identifiable risk predictor for RFS. Prevention is the key to successful management. Early identification of high risk individuals, monitoring during refeeding, and an appropriate feeding regimen is key to prevention of RFS.

Conclusion

Humans certainly have the ability to endure long periods of fasting. It has both physical and spiritual benefits. There are definite evidences for weight loss, but whether this persists once normal diet is resumed remains to be proven.

Many of the physical benefits of fasting can be achieved with intermittent fasting or calorie restriction. So for physical health reasons, longer fasts aren't advisable because of increased dangers associated with them..

Spirituality and science must come together to show logical interlinking between science and religion. The majority of research that exists on fasting is testimonial, consisting of individual personal accounts of healing without statistics or controlled scientific experiments. And therefore, there is a strong need to study physiological changes with fasting and delineate anatomical, biochemical and hormonal pathways.

Beneficial effects of fasting on human health including cognition, mental health and physical fitness, and as a treatment potential in various diseases are areas of further research. It is pertinent that we study pattern of feeding and fasting across animal kingdom including human during the evolution to develop an ideal model of health. Spiritual benefits of fasting are great and must be studied with religion and science together.

Of all the recent renewed health practices like yoga, workout, dieting and ever new practices being (re)discovered by mankind, fasting is the most natural. This is evident by the fact that every time a person wakes up from a good night of sleep, he or she has undergone a successful fast and the meal they take then is called *breakfast*!

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