

Fasting Stages

1 - Ketosis:

By 12 hours, you've entered the metabolic state called ketosis (Anton et al., Obesity 2018). In this state, your body starts to break down and burn fat.

Research:

1. Anton SD, Moehl K, Donahoo WT, Marosi K, Lee SA, Mainous AG 3rd, Leeuwenburgh C, Mattson MP. Flipping the Metabolic Switch: Understanding and Applying the Health Benefits of Fasting. *Obesity (Silver Spring)*. 2018 Feb;26(2):254-268. doi: 10.1002/oby.22065. Epub 2017 Oct 31. PMID: 29086496; PMCID: PMC5783752.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5783752/>
2. Dąbek A, Wojtala M, Pirola L, Balcerczyk A. Modulation of Cellular Biochemistry, Epigenetics and Metabolomics by Ketone Bodies. Implications of the Ketogenic Diet in the Physiology of the Organism and Pathological States. *Nutrients*. 2020 Mar 17;12(3):788. doi: 10.3390/nu12030788. PMID: 32192146; PMCID: PMC7146425.
<https://pubmed.ncbi.nlm.nih.gov/32192146/>
3. Berg JM, Tymoczko J, Stryer L. *Biochemistry*. 5th edition. New York, NY: W. H., and Freeman; 2002. Section 30.2, Each Organ Has a Unique Metabolic Profile; (2002). Available online at: <https://biokamikazi.files.wordpress.com/2013/10/biochemistry-stryer-5th-ed.pdf> [Google Scholar]

2 - Heavy Ketosis:

By 18 hours, you've switched to fat-burning mode and are generating significant ketones.

Research:

1. Anton SD, Moehl K, Donahoo WT, Marosi K, Lee SA, Mainous AG 3rd, Leeuwenburgh C, Mattson MP. Flipping the Metabolic Switch: Understanding and Applying the Health Benefits of Fasting. *Obesity (Silver Spring)*. 2018 Feb;26(2):254-268. doi: 10.1002/oby.22065. Epub 2017 Oct 31. PMID: 29086496; PMCID: PMC5783752.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5783752/>
2. Dąbek A, Wojtala M, Pirola L, Balcerczyk A. Modulation of Cellular Biochemistry, Epigenetics and Metabolomics by Ketone Bodies. Implications of the Ketogenic Diet in the Physiology of the Organism and Pathological States. *Nutrients*. 2020 Mar 17;12(3):788. doi: 10.3390/nu12030788. PMID: 32192146; PMCID: PMC7146425.
<https://pubmed.ncbi.nlm.nih.gov/32192146/>
3. Mattson MP, Longo VD, Harvie M. Impact of intermittent fasting on health and disease processes. *Ageing Res Rev*. 2017 Oct;39:46-58. doi: 10.1016/j.arr.2016.10.005. Epub 2016 Oct 31. PMID: 27810402; PMCID: MC5411330. <https://pubmed.ncbi.nlm.nih.gov/27810402/>

3 - Autophagy:

Within 24 hours, your cells are increasingly recycling old components and breaking down misfolded proteins linked to Alzheimer's and other diseases.

Research:

1. Alirezaei M, Kemball CC, Flynn CT, Wood MR, Whitton JL, Kiosses WB. Short-term fasting induces profound neuronal autophagy. *Autophagy*. 2010 Aug;6(6):702-10. doi: 10.4161/auto.6.6.12376. Epub 2010 Aug 14. PMID: 20534972; PMCID: PMC3106288. <https://pubmed.ncbi.nlm.nih.gov/20534972/>
2. Bagherniya M, Butler AE, Barreto GE, Sahebkar A. The effect of fasting or calorie restriction on autophagy induction: A review of the literature. *Ageing Res Rev*. 2018 Nov;47:183-197. doi: 10.1016/j.arr.2018.08.004. Epub 2018 Aug 30. PMID: 30172870. <https://pubmed.ncbi.nlm.nih.gov/30172870/>
3. Pietrocola F, Demont Y, Castoldi F, Enot D, Durand S, Semeraro M, Baracco EE, Pol J, Bravo-San Pedro JM, Bordenave C, Levesque S, Humeau J, Chery A, Métivier D, Madeo F, Maiuri MC, Kroemer G. Metabolic effects of fasting on human and mouse blood in vivo. *Autophagy*. 2017 Mar 4;13(3):567-578. doi: 10.1080/15548627.2016.1271513. Epub 2017 Jan 6. PMID: 28059587; PMCID: PMC5361613. <https://pubmed.ncbi.nlm.nih.gov/28059587/>
4. Vendelbo MH, Møller AB, Christensen B, Nellemann B, Clasen BF, Nair KS, Jørgensen JO, Jessen N, Møller N. Fasting increases human skeletal muscle net phenylalanine release and this is associated with decreased mTOR signaling. *PLoS One*. 2014 Jul 14;9(7):e102031. doi: 10.1371/journal.pone.0102031. PMID: 25020061; PMCID: PMC4096723. <https://pubmed.ncbi.nlm.nih.gov/25020061/>
5. Bagherniya M, Butler AE, Barreto GE, Sahebkar A. The effect of fasting or calorie restriction on autophagy induction: A review of the literature. *Ageing Res Rev*. 2018 Nov;47:183-197. doi: 10.1016/j.arr.2018.08.004. Epub 2018 Aug 30. PMID: 30172870. <https://pubmed.ncbi.nlm.nih.gov/30172870/>
6. Martin DD, Ladha S, Ehrnhoefer DE, Hayden MR. Autophagy in Huntington disease and huntingtin in autophagy. *Trends Neurosci*. 2015 Jan;38(1):26-35. doi: 10.1016/j.tins.2014.09.003. Epub 2014 Oct 2. PMID: 25282404. <https://pubmed.ncbi.nlm.nih.gov/25282404/>
7. He C, Sumpter R Jr, Levine B. Exercise induces autophagy in peripheral tissues and in the brain. *Autophagy*. 2012 Oct;8(10):1548-51. doi: 10.4161/auto.21327. Epub 2012 Aug 15. PMID: 22892563; PMCID: PMC3463459. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3463459/>
8. Wang L, Wang J, Cretoiu D, Li G, Xiao J. Exercise-mediated regulation of autophagy in the cardiovascular system. *J Sport Health Sci*. 2020 May;9(3):203-210. doi: 10.1016/j.jshs.2019.10.001. Epub 2019 Oct 15. PMID: 32444145; PMCID: PMC7242217. <https://pubmed.ncbi.nlm.nih.gov/32444145/>
9. Escobar KA, Cole NH, Mermier CM, VanDusseldorp TA. Autophagy and aging: Maintaining the proteome through exercise and caloric restriction. *Aging Cell*. 2019 Feb;18(1):e12876. doi: 10.1111/accel.12876. Epub 2018 Nov 15. PMID: 30430746; PMCID: PMC6351830. <https://pubmed.ncbi.nlm.nih.gov/30430746/>
10. Schwalm C, Jamart C, Benoit N, Naslain D, Prémont C, Prévét J, Van Thienen R, Deldicque L, Francaux M. Activation of autophagy in human skeletal muscle is dependent on exercise

- intensity and AMPK activation. *FASEB J.* 2015 Aug;29(8):3515-26. doi: 10.1096/fj.14-267187. Epub 2015 May 8. PMID: 25957282. <https://pubmed.ncbi.nlm.nih.gov/25957282/>
11. Escobar KA, Cole NH, Mermier CM, VanDusseldorp TA. Autophagy and aging: Maintaining the proteome through exercise and caloric restriction. *Aging Cell.* 2019 Feb;18(1):e12876. doi: 10.1111/accel.12876. Epub 2018 Nov 15. PMID: 30430746; PMCID: PMC6351830. <https://pubmed.ncbi.nlm.nih.gov/30430746/>

4 – Peak GH:

By 48 hours without calories or with very few calories, carbs or protein, your growth hormone level is up to five times as high as when you started your fast.

Research:

1. Hartman ML, Veldhuis JD, Johnson ML, Lee MM, Alberti KG, Samojlik E, Thorner MO. Augmented growth hormone (GH) secretory burst frequency and amplitude mediate enhanced GH secretion during a two-day fast in normal men. *J Clin Endocrinol Metab.* 1992 Apr;74(4):757-65. doi: 10.1210/jcem.74.4.1548337. PMID: 1548337. <https://pubmed.ncbi.nlm.nih.gov/1548337/>
2. Amole N, Unniappan S. Fasting induces preproghrelin mRNA expression in the brain and gut of zebrafish, *Danio rerio*. *Gen Comp Endocrinol.* 2009 Mar;161(1):133-7. doi: 10.1016/j.ygcen.2008.11.002. Epub 2008 Nov 8. PMID: 19027742. <https://pubmed.ncbi.nlm.nih.gov/19027742/>
3. Rudman D, Feller AG, Nagraj HS, Gergans GA, Lalitha PY, Goldberg AF, Schlenker RA, Cohn L, Rudman IW, Mattson DE. Effects of human growth hormone in men over 60 years old. *N Engl J Med.* 1990 Jul 5;323(1):1-6. doi: 10.1056/NEJM199007053230101. PMID: 2355952. <https://pubmed.ncbi.nlm.nih.gov/2355952/>
4. Aguiar-Oliveira MH, Bartke A. Growth Hormone Deficiency: Health and Longevity. *Endocr Rev.* 2019 Apr 1;40(2):575-601. doi: 10.1210/er.2018-00216. PMID: 30576428; PMCID: PMC6416709. <https://pubmed.ncbi.nlm.nih.gov/30576428/>
5. Caicedo D, Díaz O, Devesa P, Devesa J. Growth Hormone (GH) and Cardiovascular System. *Int J Mol Sci.* 2018 Jan 18;19(1):290. doi: 10.3390/ijms19010290. PMID: 29346331; PMCID: PMC5796235. <https://pubmed.ncbi.nlm.nih.gov/29346331/>

5 – Minimum Insulin:

By 54 hours, your insulin has dropped to its lowest level point since you started fasting and your body is becoming increasingly insulin-sensitive.

Research:

1. Klein S, Sakurai Y, Romijn JA, Carroll RM. Progressive alterations in lipid and glucose metabolism during short-term fasting in young adult men. *Am J Physiol.* 1993

Nov;265(5 Pt 1):E801-6. doi: 10.1152/ajpendo.1993.265.5.E801. PMID: 8238506.

<https://pubmed.ncbi.nlm.nih.gov/8238506/>

2. Gjedsted, Jakob & Gormsen, Lars & Nielsen, Søren & Schmitz, O & Djurhuus, Christian & Keiding, Susanne & Ørskov, H & Tønnesen, Else & Møller, Niels. (2007). Effects of a 3-day fast on regional lipid and glucose metabolism in human skeletal muscle and adipose tissue. *Acta physiologica (Oxford, England)*. 191. 205-16. 10.1111/j.1748-1716.2007.01740.x.
www.researchgate.net/publication/6055419_Effects_of_a_3-day_fast_on_regional_lipid_and_glucose_metabolism_in_human_skeletal_muscle_and_adipose_tissue

6 – Immune Regeneration:

By 72 hours, your body is breaking down old immune cells and generating new ones insulin-sensitive.

Research:

1. Cheng CW, Adams GB, Perin L, Wei M, Zhou X, Lam BS, Da Sacco S, Mirisola M, Quinn DI, Dorff TB, Kopchick JJ, Longo VD. Prolonged fasting reduces IGF-1/PKA to promote hematopoietic-stem-cell-based regeneration and reverse immunosuppression. *Cell Stem Cell*. 2014 Jun 5;14(6):810-23. doi: 10.1016/j.stem.2014.04.014. Erratum in: *Cell Stem Cell*. 2016 Feb 4;18(2):291-2. PMID: 24905167; PMCID: PMC4102383.
<https://pubmed.ncbi.nlm.nih.gov/24905167/>

Breaking a Fast

It's best to break your fast with a balanced meal including plenty of vegetables, plant fibers and plant fats, with healthy proteins and some whole grains or legumes if you choose. Avoid simple sugars and processed/packaged foods. Learn what works best for your body, and what you feel best eating following your fasts.

Research:

1. Mattson MP, Moehl K, Ghena N, Schmaedick M, Cheng A. Intermittent metabolic switching, neuroplasticity and brain health. *Nat Rev Neurosci*. 2018 Feb;19(2):63-80. doi: 10.1038/nrn.2017.156. Epub 2018 Jan 11. Erratum in: *Nat Rev Neurosci*. 2020 Aug;21(8):445. PMID: 29321682; PMCID: PMC5913738.
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5913738/>

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