

Casual Friday Presents

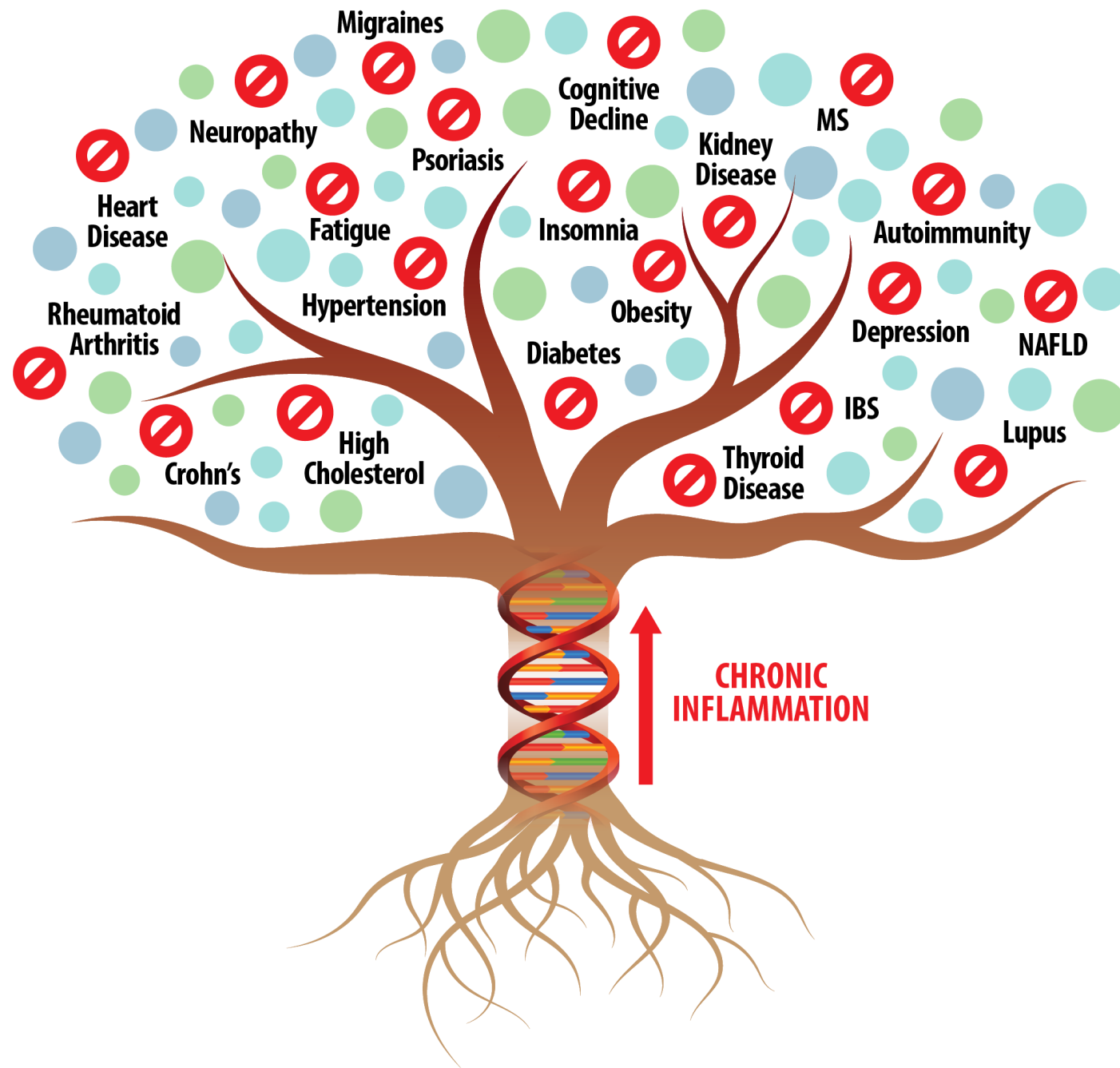
Chronic Migraine

FM Strategies: Physiology, Pathology, Interventions.

A BIOGENETIX CLINICAL PRESENTATION

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The International Classification of Headache Disorders, 3rd edition (ICHD-3) :

Migraine without aura: At least 5 attacks lasting 4–72 hours untreated or unsuccessfully treated. The headache has at least 2 of these features: one-sided location, pulsating quality, moderate or severe intensity, or worsening with ordinary activity. During the headache, there is either nausea/vomiting or both light and sound sensitivity.

- Migraine with aura: At least 2 attacks with fully reversible neurologic symptoms, commonly visual, sensory, or speech/language symptoms. Typical aura features gradual development; individual symptoms usually last 5–60 minutes.
- Chronic migraine: Headache on 15 or more days/month for over 3 months, with a prior history of migraine and migraine features or migraine-specific treatment response on at least 8 days/month.
- Medication-overuse headache (MOH): Headache on 15 or more days/month in someone with a pre-existing headache disorder, with regular overuse of acute headache medication for over 3 months. The overuse threshold is generally 10 or 15 medication days/month, depending on the medication class.
- Status migrainosus: A debilitating migraine attack lasting more than 72 hours.

PubMed references

1. Headache Classification Committee of the International Headache Society (IHS). *The International Classification of Headache Disorders, 3rd edition. Cephalalgia*. 2018;38(1):1–211. PMID: 29368949. [PubMed](#)
2. Kebede T, et al. *Medication overuse headache: a review of current evidence and management strategies*. 2023. PMID: 37614243. [PubMed](#)
3. *Status migrainosus*. 2024. PMID: 38307660. [PubMed](#)

Temporomandibular Joint (TMJ):

Pain at the temples, in front of the ears.



Sinusitis: Pain behind the brow bone and/or cheekbones.



Cluster: Pain in and around one eye.



Tension: Pain is like a band squeezing the head.



Migraine: Pain (one sided), Nausea and visual changes.



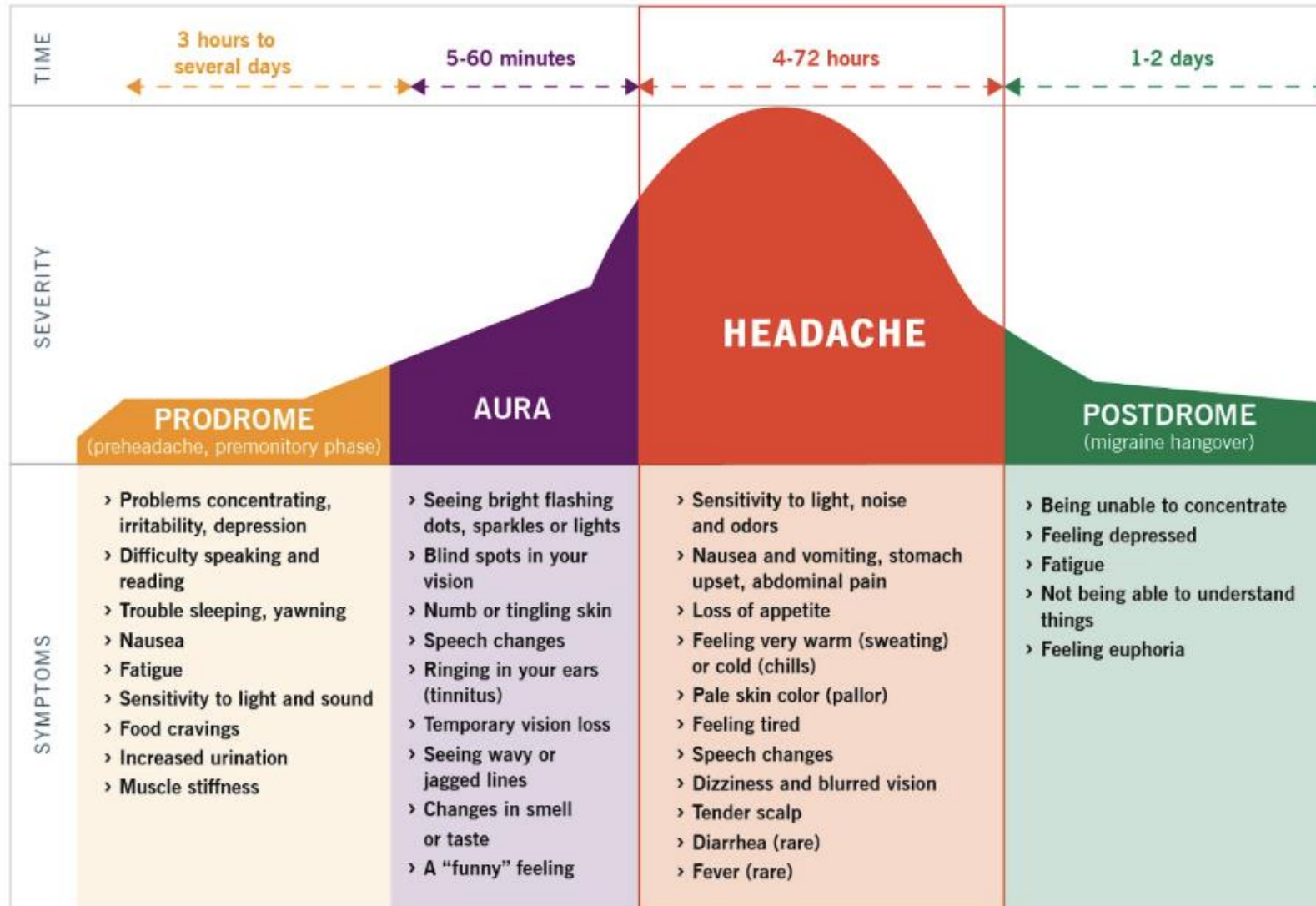
Cervicogenic (referred from the neck): Pain is at the top and/or back of the head.



Medication-overuse headache (MOH): dull constant pain, often worse in the morning.

<https://doc.vortal.com/chilidsites/uploads/308/files/headache-types.png>

The 4 Phases of a Migraine Headache



21-MEU-2074429

Toxic Migraine



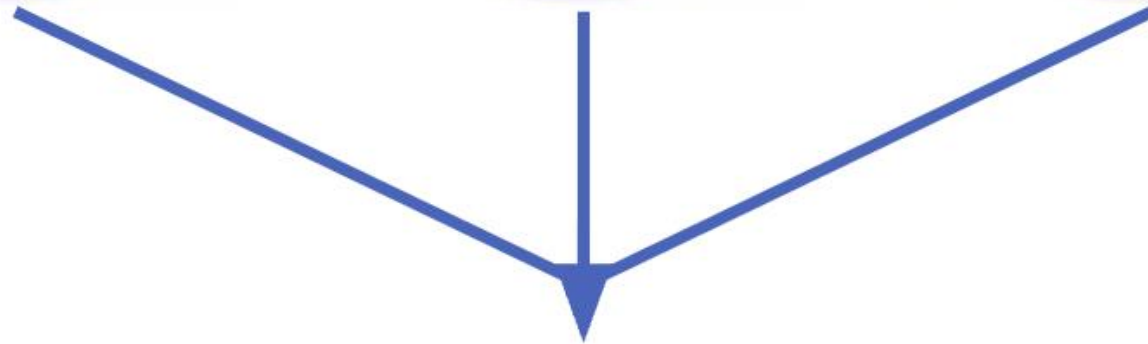
Mechanical



Chemical



Psychological



Biogenetix™

3 Application Targets

1. Magnesium
2. FRAP (Ferric Reducing Antioxidant Power)
3. MDA Control (Malondialdehyde)



Magnesium and Migraine

[Ligia J Dominguez](#) ^{1,*}, [Nicola Veronese](#) ², [Shaun Sabico](#) ³, [Nasser M Al-Daghri](#) ³, [Mario Barbagallo](#) ²

Although the pathophysiology of migraine is still not completely clear, in recent years there have been important advances in knowledge about mechanisms that help explain it and new therapeutic targets that have led to the availability of new pharmacological treatments [7]. However, there are also dietary components and other environmental determinants that seem to contribute to the genesis of migraine, including magnesium insufficiency.

Magnesium is a crucial mineral that plays an essential role in numerous cellular functions, including over 600 enzymatic reactions, energy production, oxidative phosphorylation, protein synthesis, nucleic acid synthesis and stability, and carbohydrate metabolism [8,9,10,11]. Maintaining adequate magnesium levels is vital for the proper functioning of organs and systems in the human body, including the nervous system. Magnesium deficiency is prevalent in older adults and has been linked to several age-related chronic conditions and other diseases such as migraine [11,12,13].

Magnesium and Migraine

[Ligia J Dominguez](#) ^{1,*}, [Nicola Veronese](#) ², [Shaun Sabico](#) ³, [Nasser M Al-Daghri](#) ³, [Mario Barbagallo](#) ²

Editor: Christopher Bell

Several studies have indicated a link between magnesium deficiency and headaches. Lower concentrations of magnesium have been reported in migraine patients in the serum [67,68] and saliva [68], intracellularly in erythrocytes and lymphocytes [69], and in both ictal and interictal brain regions in MR spectroscopy assessments [70]. Similar findings have been reported in other case–control studies [71,72,73]. A study utilizing a magnesium load test revealed increased magnesium retention in migraine sufferers compared to healthy controls, suggesting a systemic magnesium deficiency linked to migraine [71]. Additionally, a two-week trial showed that when migraine patients consumed mineral water with 110 mg/L of magnesium daily (ranging from 7.4 to 12 mmol per day for 15–18 days), their intracellular erythrocyte magnesium concentrations significantly increased, compared to those in healthy controls [69].

► [Nutrients](#). 2025 Feb 18;17(4):725. doi: [10.3390/nu17040725](#) 

Mag

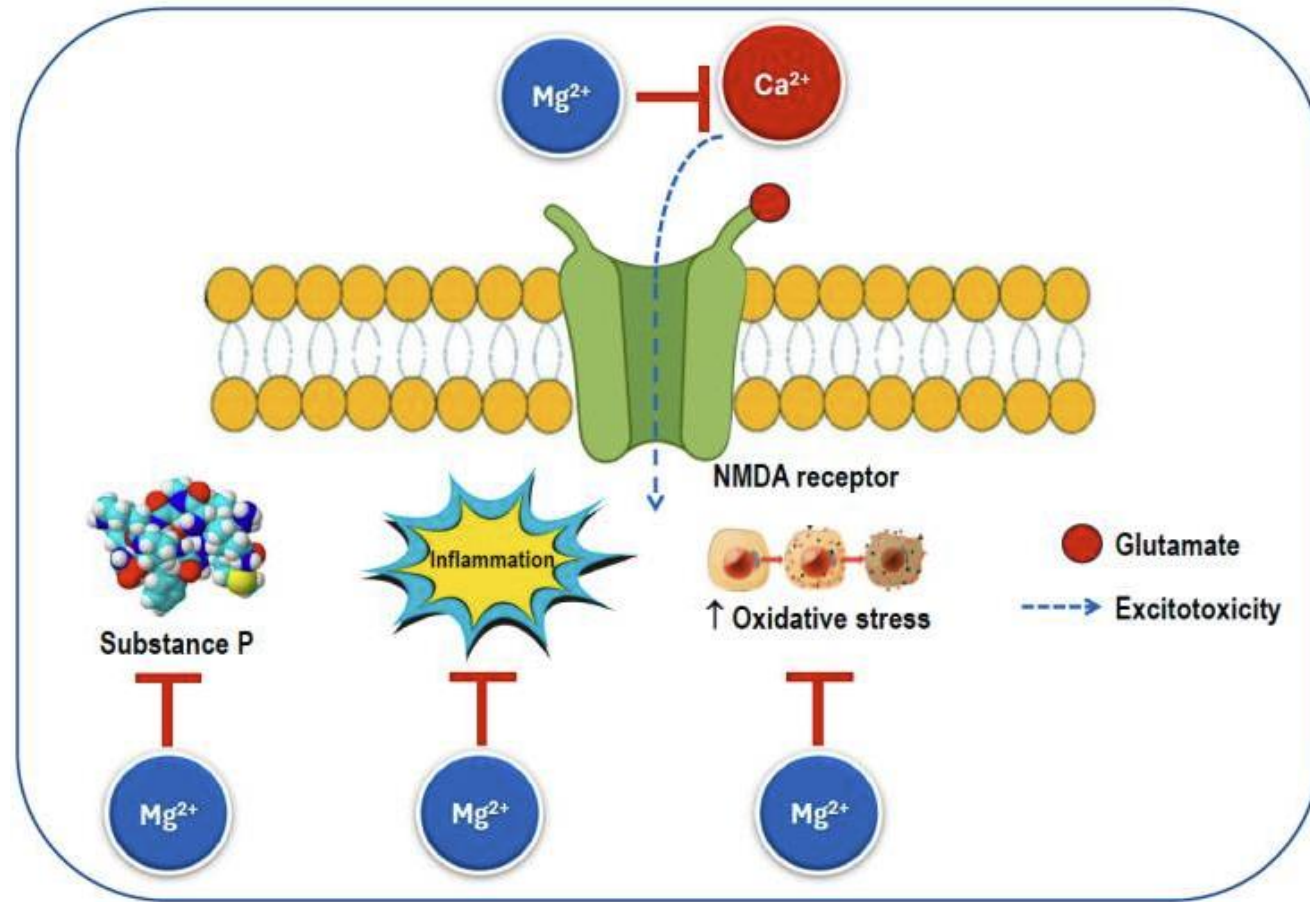
[Ligia J](#)

Editor

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PMCID

A study found that low serum magnesium levels caused a 35-fold increase in the likelihood of acute headaches in migraine patients [73]. This suggests that magnesium deficiency is an independent risk factor for the onset of migraines. Similarly, a study examined the relationship between clinical responses to 1 g of intravenous magnesium sulfate infusion for acute migraine and baseline serum ionized magnesium levels. The authors found a 50% pain reduction following the infusion in 87.5% of all participants with acute migraine, regardless of their serum magnesium level; however, in 86% of the patients with magnesium levels below 0.54 mmol/L, the relief lasted at least 24 h compared to 16% of those with serum ionized magnesium levels above 0.54 mmol/L [74]. Together, these findings support a link between magnesium deficiency and migraine and suggest magnesium deficiency as an independent risk factor for migraine occurrence. However, other research studies have found normal magnesium levels in the blood serum of migraine sufferers [75,76]. Interestingly, a study found that while the magnesium levels were within the normal range in patients with migraine and age-matched healthy controls, electrophysiological tests revealed abnormalities typically associated with hypomagnesemia [75]. The authors proposed a potential link between the frequency and severity of migraines and disturbances in neuromuscular excitability that depend on intracellular magnesium levels rather than on serum magnesium concentrations. Indeed, magnesium is a predominantly intracellular ion, while blood serum only contains about 1–2% of the total body magnesium [11]. The intracellular magnesium levels do not necessarily correlate with the overall serum magnesium levels: low intracellular magnesium has been found even in the absence of altered total serum magnesium [19,48,49,50]. A study found that in migraine patients with low intracellular erythrocyte and lymphocyte magnesium concentrations, the serum levels were normal [69]. In another study,



Possible mechanisms for the beneficial effects of magnesium on migraine. An excess of calcium influx through the NMDA receptor increases excitotoxicity, which triggers substance P release, inflammation, and oxidative stress. The magnesium ion blocks the ion channel of the NMDA receptor inhibiting calcium influx and preventing its excessive activation. NMDA: N-methyl-D-aspartate.

Takeaway:

600mg/day, citrate or otherwise.

Days to weeks.

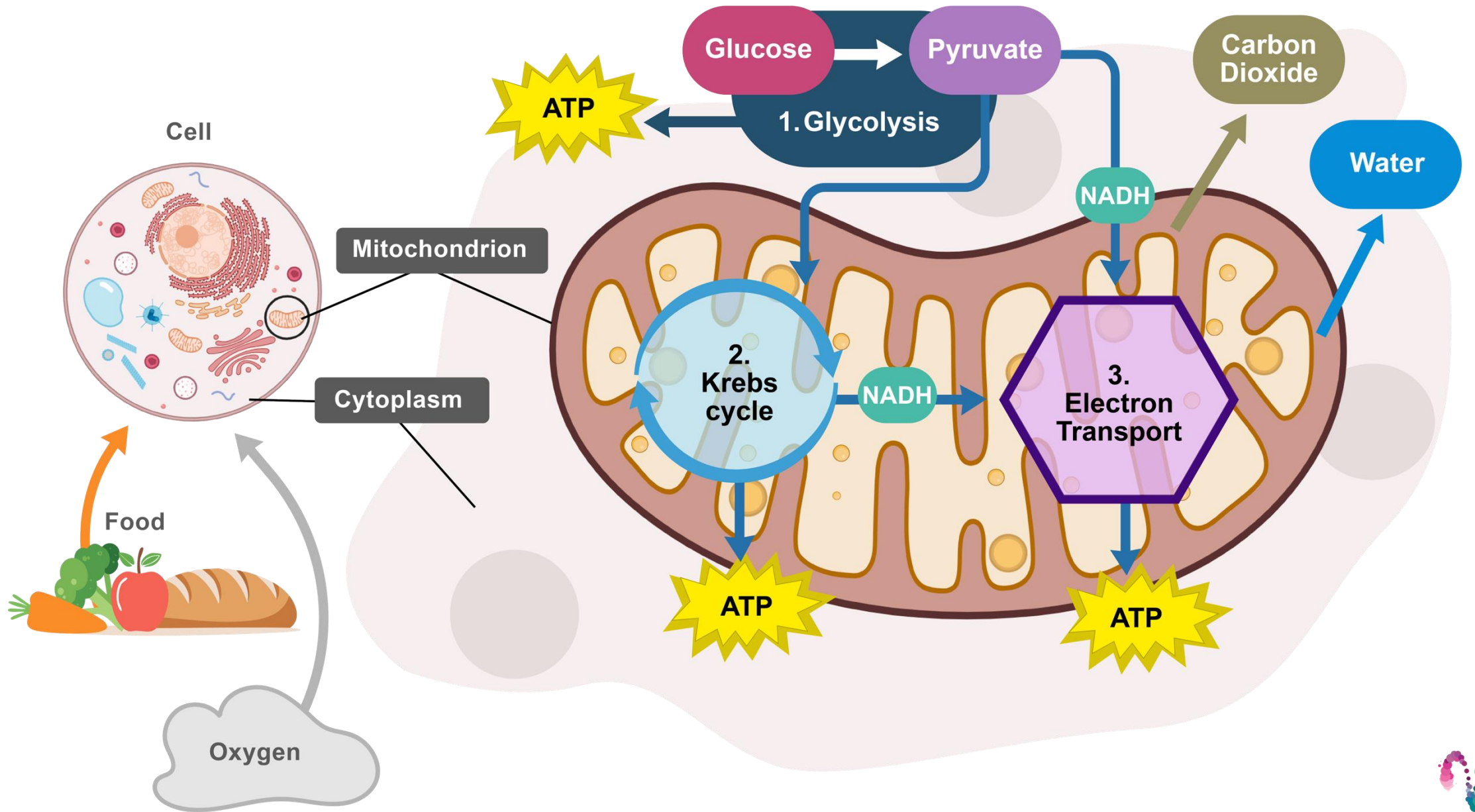
Prevent Mg deficiency or expenditure otherwise.

Oxidative Stress and Migraine

Félix Javier Jiménez-Jiménez ¹, Hortensia Alonso-Navarro ², Elena García-Martín ³,
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The pathogenesis of migraine is not completely understood, but inflammation and oxidative stress seem to be involved, according to data from an experimental model of the disease. This narrative review summarizes data from studies on oxidative stress markers in migraine patients, case-control association studies on the possible association of candidate genes related to oxidative stress with the risk for migraine, studies showing the presence of oxidative stress in experimental models of migraine, and studies on the efficacy of antioxidant drugs in migraine therapy. Many studies have addressed the value of concentrations of prooxidant and antioxidant substances or the activity of antioxidant enzymes in different tissues (mainly in serum/plasma or in blood cells) as possible biomarkers for migraine, being thiobarbituric acid (TBA) reactive substances (TBARS) such as malonyl dialdehyde acid (MDA) and 4-hydroxynonenal, and nitric oxide (this at least during migraine attacks in patients with migraine with aura (MWA) the most reliable. In addition, the possible usefulness of antioxidant treatment is not well established, although preliminary short-term studies suggest a beneficial action of some of them such as Coenzyme Q₁₀ and riboflavin. Both topics require further prospective, multicenter studies with a long-term follow-up period involving a large number of migraine patients and controls.





FRAP

FRAP (Ferric-Reducing Antioxidant Power): A measure of the total non-enzymatic antioxidant capacity in blood plasma. FRAP and overall antioxidant defenses are typically reduced in chronic migraine sufferers and during active oxidative shifts, reflecting a depleted capacity to neutralize free radicals.

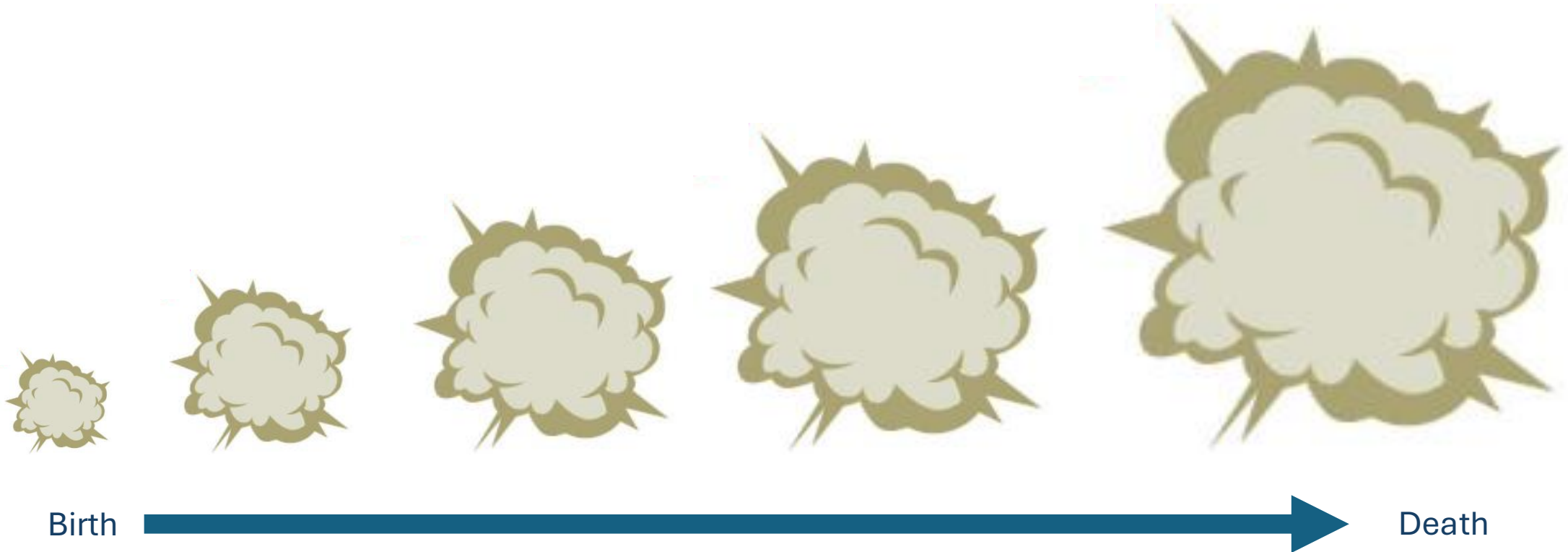
*The Caveat.

MDA

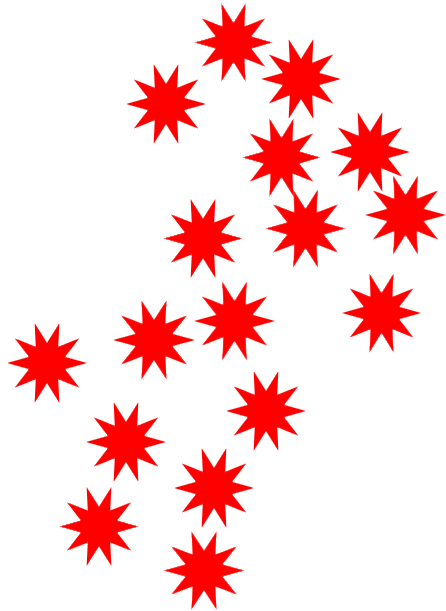
High malondialdehyde (MDA) levels occur in individuals experiencing significant oxidative stress and cellular inflammation. Because MDA is a direct byproduct of lipid peroxidation (free radicals attacking fat molecules in cell membranes), elevated levels are a non-specific signal that tissues are undergoing ongoing oxidative damage.

*The Caveat.

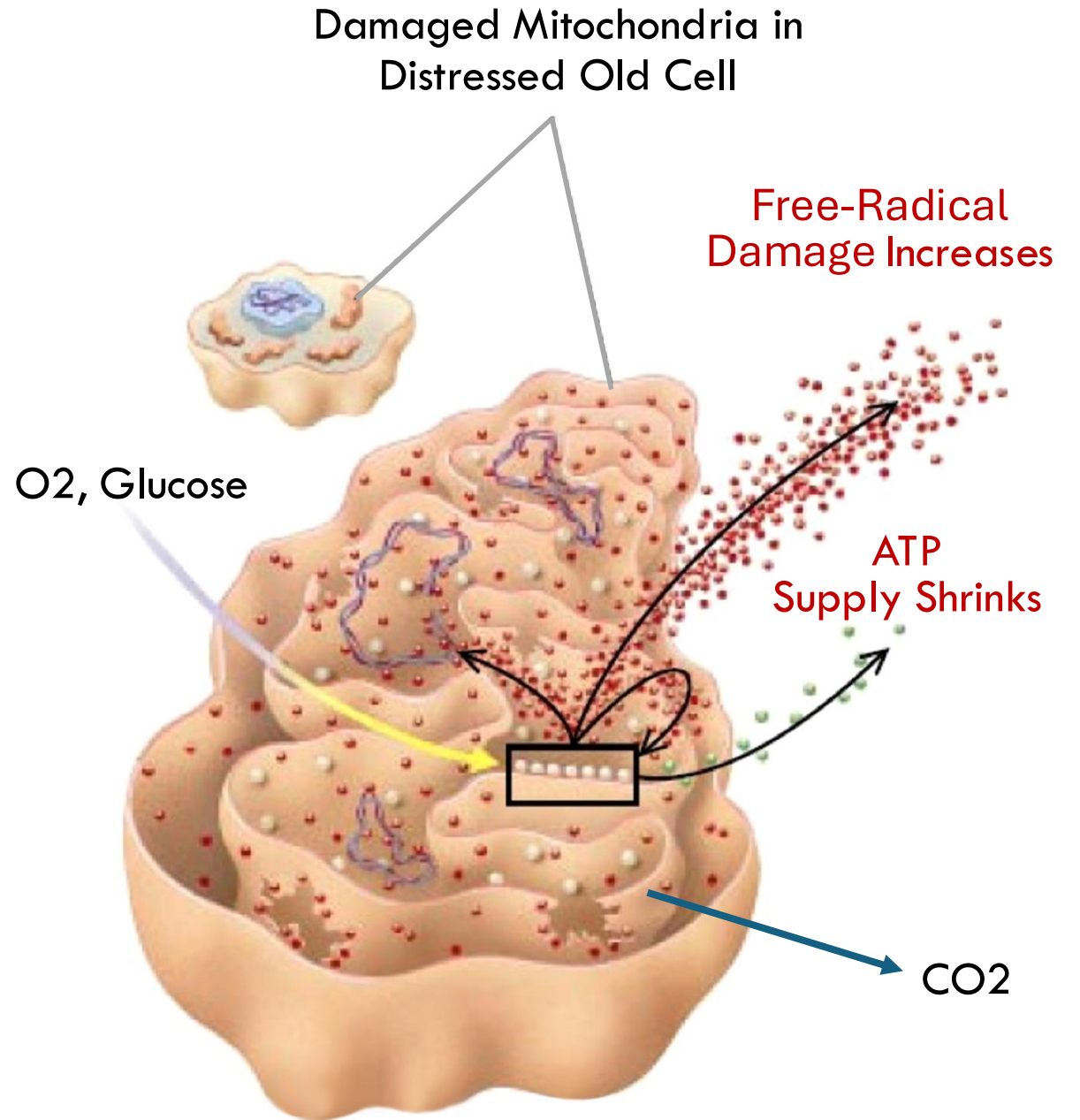
The Antigenic Cloud



 = Glucose Molecule



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Chronic Metabolic & Inflammatory Diseases

- **Type 2 diabetes:** Chronic high blood sugar drives rapid free radical production, leading to systemic lipid damage.
- **Cardiovascular diseases:** High levels are strongly linked to atherosclerosis, hypertension, and advanced heart disease.
- **Autoimmune disorders:** Elevated levels are found in individuals with rheumatoid arthritis and systemic lupus erythematosus (SLE) due to overactive immune responses.
- **Liver and gut diseases:** High levels track closely with fatty liver disease (MASLD) and inflammatory bowel disease (IBD).
- **Advanced cancers:** Tumor progression and cellular transformation are consistently associated with heightened tissue and circulating MDA.

Acute Conditions

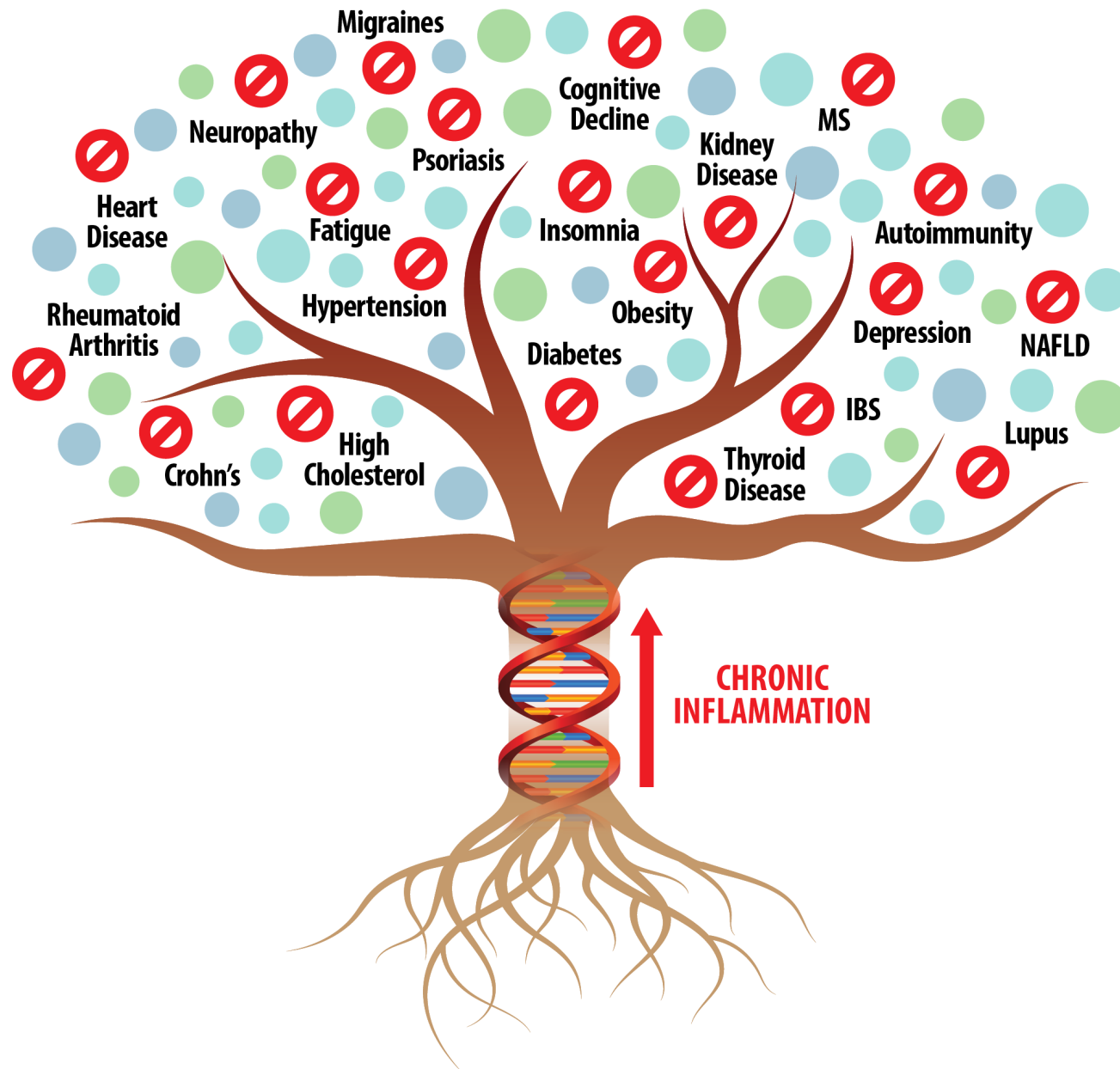
- **Ischemic stroke:** Sudden tissue damage and oxygen deprivation cause immediate spikes in lipid peroxidation.
- **Sepsis:** Severe, full-body infections trigger profound systemic inflammation and a massive surge in oxidative markers.

Lifestyle & Environmental Factors

- **Tobacco smoking:** Inhaling cigarette smoke introduces immense amounts of direct oxidants into the bloodstream.
- **Poor dietary habits:** Diets heavy in ultra-processed foods, refined sugars, and industrial trans-fats accelerate cellular lipid damage.
- **Extreme overtraining:** Excessive physical exertion without proper rest overpowers the body's natural antioxidant defenses.
- **Toxin exposure:** Chronic contact with severe air pollution, heavy metals, or environmental chemicals rapidly depletes antioxidant reserves.

So what are our options?

Magnesium, and...



Alpha lipoic acid
Glutathione
Resveratrol
NAC
Riboflavin
CoQ10
Quercetin

We Want to Hear from You!

Give us your Casual Friday feedback
with this short 5-question survey.



biogenetix.com/survey