# Vitamin C and Magnesium: The Master Supplements

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## The Cause of All Disease: A Unified Theory

The onset and evolution of **all** diseases, as well as all of the associated symptomatology, is caused by, and/or mediated by:

**Increased**

**Intracellular Oxidative Stress (IOS)**

Increased IOS exists when the production of free radicals (highly reactive pro-oxidants) exceeds the body's antioxidant capacity to neutralize (reduce) them, or to prevent their production in the first place. Elevated IOS **always** exists where there is a deficiency of antioxidants, an excess of free radicals, or both [16760481].

## Redox Medicine Basics

All disease, regardless of the tissues or organs involved, results from the relative ***presence of*** and the ***interactions among and between***:

**Pro-Oxidants (Toxins)**

**Pathogens (MAJOR Pro-Oxidant *Providers*)**

**Antioxidants (Nutrients)**

## Reference Checking

**Go to:**

http://www.ncbi.nlm.nih.gov/pubmed/

In the PubMed search box, enter the seven or eight digit number, by itself, at the end of each reference in this presentation. This is the PubMed Identifier (PMID) number

Then click on "Search" and you will go directly to the Abstract of that article, or for a few articles, you will have access to the full article. If there is no PMID number, it is not available on PubMed.

## Redox Medicine Basics

The essence of redox (reduction-oxidation) medicine is really the essence of vitamin C-based biochemistry.

**Pro-oxidant** (aka "toxin")

Takes, or causes to be taken, electrons away from reduced (normal) biomolecules (OXIDATION)

**Antioxidant** (vitamin C is the prototype)

Gives (or restores) electrons back to oxidized biomolecules (REDUCTION)

## Redox Medicine Basics

The basic redox nature of vitamin C and the pro-oxidant nature of all toxins concisely explains why vitamin C, along with many other antioxidants, has been documented to be an effective ***antitoxin*** against ***all*** toxins for which it has been tested, *in vitro* and *in vivo*, in plants, animals, and humans, and including clinical studies.

## Redox Medicine Basics

Even though there is a tremendous variety of molecular structure among all of the known toxins, they ALL SHARE the property of taking, or causing to be taken, electrons from other molecules, oxidizing them and resulting in a state of increased oxidative stress.

If a molecule does not cause the loss of one or more electrons from another molecule it IS NOT TOXIC, and it CANNOT BE TOXIC. Toxicity and any symptoms of toxicity cannot exist unless electrons are being taken from other molecules (oxidation).

## Redox Medicine Basics

Whether cells, tissues, and organs are healthy is **simple**: are a preponderance of the constituent biomolecules oxidized or not? The nature and degree of the disease depends on:

1. **Which** biomolecules are oxidized?
2. **Where** are they located?
3. **Degree**: Is the percent of oxidized biomolecules minimal, moderate, or advanced?
4. **Duration**: How long have those biomolecules been oxidized?

On the other hand, the many ways that pro-oxidants (toxins) are introduced into the body, along with the biochemical pathways and reactions that are impaired or blocked in the course of increasing the numbers of oxidized biomolecules, is almost incomprehensibly **complex**.

## Toxin Characteristics

7. Tendency to target specific enzymes, amino acids, antioxidants, and antioxidant enzymes
8. Tendency to physically accumulate and block critical biomolecules from interacting
9. Toxin similarity to structural biomolecules (replacement, incorporation)
10. Access to excretion by chelation
11. Access to excretion without chelation
12. Access to excretion by sweating

## Redox Medicine Basics

All disease, then, **IS** increased oxidative stress.

Biomolecules (nucleic acid, proteins, enzymes, sugars, fats, etc.) are **inactive or less active when oxidized**, and **optimally active when reduced**.

Therefore, the unique nature of any disease process depends solely on how many biomolecules are oxidized and where they are located and concentrated, nothing more. In other words, **any** disease depends on the degree to which vital biomolecules have become inactivated (oxidized).

## Toxin Characteristics

1. Solubility properties (fat, water, combination)
2. Molecular size (physical access)
3. Ionic charge, neutrality
4. Unique molecular structure (physical fit)
5. How readily it oxidizes certain biomolecules
6. Tendency to produce oxidative chain reactions or to oxidize single biomolecules

## Prominent Promoters of Chronic Degenerative Diseases

1. Infections (endotoxins, exotoxins, aerobic and anaerobic metabolic byproducts, **dental**); documented to strongly promote oxidative stress and lessen antioxidant capacity; focal infections anywhere in the body
2. Chronic pathogen colonization (especially sinus, pharynx, and upper respiratory tract); probably a **MAJOR** reason for gut dysfunction/disease
3. Known exogenous toxin exposures (heavy metal, pesticides, etc.)
4. Toxic **iron** status (most people in "normal" range are toxic); also calcium and copper
5. Dietary toxin exposures (constipated gut, *Clostridium*); inadequate/poor nutrition and/or poor digestion; poor digestion is **worse** than poor nutrition in terms of overall negative impact on the antioxidant capacity of the body
6. Hormone imbalances (sex, cortisol, **thyroid**)

## Intracellular Oxidative Stress Modulators

The primary characteristic of any disease, infection, or intoxication at the cellular level is **increased intracellular oxidative stress (increased IOS)**. If IOS is not elevated, there is no disease or pathology. If it is present, then some disease or pathology does exist. Increased IOS is the ***sine qua non*** of all illness.

The primary determinants of this intracellular oxidative stress status are the intracellular levels of:

1. Calcium
2. Magnesium
3. Vitamin C
4. Glutathione

## Intracellular Oxidative Stress Modulators

**Magnesium**:

When intracellular calcium levels are high, magnesium levels are low. As more magnesium goes into the cell, more calcium comes out. Magnesium is a natural calcium channel blocker and a general calcium metabolism antagonist. This is likely the single most important property of magnesium in terms of its ***enormous*** positive health impact throughout the body. When intracellular magnesium levels are normal, there is no increased IOS, and the cell is physiologically normal. And when enough cells in a diseased tissue or organ can regain a normal level of IOS, **there is no longer any disease**.

Just as extra calcium **increases** all-cause mortality, more magnesium **decreases** all-cause mortality [18271493, 21703623]

## Intracellular Oxidative Stress Modulators

**Glutathione (GSH)**:

While technically the most concentrated and physiologically important of intracellular antioxidants, glutathione levels will never be normal when calcium is up, magnesium is down, and vitamin C is down. The synthesis and maintenance of normal levels of GSH synthesis, along with normal GSH metabolism can only occur as the levels of these other three agents normalize, and increased oxidative stress can no longer impede intracellular GSH synthesis. Supporting GSH synthesis with supplementation of precursors is beneficial, but the **main support** of normal GSH levels and metabolism comes only when calcium, magnesium, and vitamin C levels are normal or approaching normal.

## Intracellular Oxidative Stress Modulators

**Calcium**:

The intracellular calcium concentration is the primary determinant **and** marker of increased IOS. The higher the level, the greater the IOS. When the level is normal there is no longer excessive IOS and the cell physiology is in a normal state. **The manipulation of intracellular calcium levels appears to be the most straightforward way to positively impact IOS, and *thereby* positively impact all disease processes**.

Increased calcium intake by both supplemental and dietary sources dramatically increases all-cause mortality (death from any disease) [23403980]. Calcium supplementation has also been shown to significantly increase the risk of heart attack [22626900, 20671013]

## Intracellular Oxidative Stress Modulators

**Vitamin C**:

When intracellular calcium levels are high and intracellular magnesium levels are low, vitamin C levels are always low as well. The delivery of more vitamin C inside cells further promotes increased magnesium levels and decreased calcium levels. There is always an **ongoing dynamic interplay** between calcium, magnesium, and vitamin C in the intracellular space.

Whenever IOS is severely and chronically elevated, a state of intracellular scurvy can effectively be considered to be present.

## Hormones and Oxidative Stress

A good way to categorize hormones and their function conceptually is to realize that they all serve two main purposes: They work to:

1. Positively modulate normal metabolism (optimize and accelerate), and
2. Minimize/normalize increased intracellular oxidative stress (increased IOS).

Even though different hormones have widely differing biochemical impact, **they all share these two primary purposes**.

## Hormones and Oxidative Stress

**Insulin, hydrocortisone, thyroid hormone, and sex hormone(s)** are four of the body's most important hormones.

While technically not hormones, both vitamin C and magnesium are essential for the optimal functioning of **every** cell in the body. As such, it is suggested that along with the four important hormones mentioned above, it is **probably most accurate to think of vitamin C and magnesium *functionally* as two additional vital hormones** for the body, as no cell functions properly when their levels are depleted.

Always think of combinations of the above six agents in treating nearly all medical conditions, including infections.

## The Final Common Denominator

When vitamin C levels are normal inside the cell, IOS by definition is at normal, physiological levels, and the cell is as "normal" as it is going to get. And even though many conditions can be effectively treated with the chronic administration of high doses of vitamin C, it is not the only way to optimize intracellular levels of vitamin C. And, indeed, in some conditions, high doses of vitamin C **ALONE** will never optimize these intracellular vitamin C levels without addressing other factors and without administering other agents.

## Hormones and IOS

**Estrogen**:

1. Serves as a calcium channel blocker [19389388]
2. Serves to effectively raise intracellular magnesium levels [3227989]
3. Promotes magnesium retention via renal tubular reabsorption before urinary elimination [18949482]
4. Powerful anti-inflammatory agent [30671410]
5. Lessens metabolic syndrome parameters and dramatically decreases all-cause mortality [9116097]

## The Final Common Denominator

Remember that the GOAL of all optimally effective clinical protocols is to normalize the increased IOS that is characteristic of ALL diseased cells, and therefore, all diseases and medical conditions. When this is accomplished, the cell is NO LONGER diseased, since it is the presence and degree of oxidized biomolecules that determines whether disease exists, NOTHING MORE.

## Agents Optimizing Vitamin C/Antioxidant Status

Some of the most critical factors in optimizing intracellular vitamin C levels include the following:

1. Optimal levels of critical hormones (estrogen, testosterone, thyroid, insulin, hydrocortisone)
2. Elimination of focal infection or containment of those foci (usually dental)
3. Optimal body-wide levels of magnesium (intracellular most important)
4. Optimal digestion (minimizing putrefaction)
5. Optimal additional supplementation

## Hormones and IOS

**Testosterone**:

1. Serves as a calcium channel blocker [16527846]
2. Powerful anti-inflammatory agent [20589735]
3. Lessens metabolic syndrome parameters and decreases all-cause mortality [26248567]
4. Lessens insulin resistance and possibly facilitates cellular magnesium uptake
5. Helps to optimize the function of other hormones

## Hormones and IOS

**Insulin**:

1. Powerful healing agent in local and systemic applications [5635406, 28263805]
2. Directly promotes **cellular magnesium uptake** [771414]
3. Directly promotes **cellular vitamin C uptake** [9550452]
4. Serves to conserve (reabsorb) magnesium in the kidney before urinary elimination [10600938]
5. Optimizes glucose metabolism by facilitating cellular glucose uptake; intracellular glucose metabolism then supported by a normal redox state (normal IOS levels) facilitated by better Mg and VC levels in cytoplasm

## Hormones and IOS

**Thyroid hormone**:

1. Probably the most powerful modulator/suppressor of increased body-wide oxidative stress, facilitating the normalizing of IOS (increased Mg, decreased Ca, increased VC) [18604605, 30294577, 31193031, 29967483]
2. Thyroid supplementation normalizes intracellular Mg in hypothyroid animals [18604605], while preventing intracellular Ca overload [16331687]. Intracellular calcium is elevated in hypothyroid state [3676598]
3. Subclinical hypothyroidism substantially increases body-wide oxidative stress (traditional thyroid testing in "normal" ranges)
4. Subclinical hypothyroidism increases the contraction of systemic infectious diseases, and it greatly facilitates the metastatic-like spread of focal infections, and probably promotes the metastatic spread of cancers as well

## Focal Infections and Redox Balance

Based on the work of Dr. Broda Barnes (subclinical hypothyroidism and massively increased heart attack/infectious disease incidence), it would appear that normalizing the status of magnesium, vitamin C, insulin, cortisol, sex hormones, and thyroid can give an enormous amount of protection against the toxicity and spread of focal infections, whether in the oral cavity or anywhere else in the body.

**Eliminating focal infections and/or keeping focal infections focal is the single most important factor in preventing the onset and evolution of disease, as well as in reversing disease that has not become too chronic.**

## Hormones and IOS

**Hydrocortisone**:

1. Powerful anti-inflammatory agent
2. Serves as a calcium channel blocker [3685396, 14656715]
3. Greatly enhances **cellular vitamin C uptake** [11502226]

## Focal Infections and Redox Balance

The most critical factors for **keeping focal infections focal** are those that minimize IOS. A healthy cell resists infection very effectively. These factors include:

1. Lowered intracellular calcium with increased intracellular magnesium
2. Increased intracellular vitamin C and GSH
3. Normal estrogen, testosterone levels
4. **Completely** normal thyroid status (euthyroid)
5. Proper ongoing testing, hormone replacement, and optimal supplementation to achieve these goals

## Optimizing IOS, VC, and Mg status

**Thyroid hormone status**:

Many individuals have intracellular cellular hypothyroidism ***not*** reflected on standard thyroid function tests, and a proper ratio of free T3 to reverse T3 needs to be achieved, as that is reflective of normalized intracellular thyroid function. These laboratory tests should always be a part of every medical and/or dental evaluation.

A majority of adults today are probably at least mildly hypothyroid; standard thyroid blood testing typically **does not reflect this**. Rather, such testing does reflect nearly any degree of **hyper**thyroidism fairly well, as well as ***severe*** **hypo**thyroidism.

## Optimizing IOS, VC, and Mg status

**Thyroid hormone status**:

Much of the reason for this is that most mildly hypothyroid individuals have ***intracellular*** (often referred to as "subclinical" hypothyroidism, **not consistently reflected in circulating thyroid hormone levels**. Only 15 to 20% of T3, the active form of thyroid hormone, is produced from T4 inside the thyroid gland, while the rest is produced in nearly all of the **cells outside of the thyroid** from circulating T4 taken up in those cells. Paradoxically, the thyroid gland should ***not*** be the focus of thyroid therapy; the many cells of the body should be that focus.

## Optimizing IOS, VC, and Mg status

Monitor thyroid therapy (dessicated thyroid) by ***symptom*** improvement, body ***temperature***, and by ***improvement/normalization*** of the free T3/reverse T3 ratio.

A consistent temperature on awakening should be 97.8 to 98.2, according to Dr. Barnes.

Aim for a ratio of 18/1 to 20/1, or slightly higher. If hypothyroid symptoms are still clear-cut, the slightly higher ratio can be maintained. But even if mild symptoms are still present, having a ratio of about 20/1 is a strong assurance that **substantial** intracellular hypothyroidism is no longer present.

## Optimizing IOS, VC, and Mg status

**Magnesium**:

Roughly 99% of the body's magnesium is intracellular, and about 95% of that is inside the mitochondria

Blood levels are irrelevant unless they are low, which clearly indicates an advanced depletion of the body's magnesium content. However, most "normal" blood magnesium levels are still seen even when there is a significant body-wide depletion of magnesium stores. If there is a question of magnesium status, probably the best test now available is the sublingual epithelial cell magnesium assay, which has correlated well with the magnesium levels seen with muscle and atrial tissue biopsies (available at www.exatest.com)

## Optimizing IOS, VC, and Mg status

**Thyroid hormone status**:

Deiodinases inside cells take off iodine molecules from T4, T3, and T2. Taking the incorrectly situated iodine molecule off T4 makes inactive, reverse T3 instead of active T3.

**Increased IOS, eventually resulting from increased oxidative stress throughout the body, inactivates deiodinases, like any other enzyme**.

As infections and chronic diseases like cancer stabilize/resolve, thyroid function can "recover" and previously adequate thyroid replacement can start inducing mild hyperthyroidism if the primary insult was increased oxidative stress and not depleted thyroid function. However, most patients who present with substantially depressed T3 levels along with the reverse T3 elevations will probably need replacement therapy for life, although it will need to be periodically adjusted as generalized oxidative stress is minimized.

## Optimizing IOS, VC, and Mg status

Example:

Free T3 (triiodothyronine): 3.1 pg/mL (reference range: 2.0-4.4)

Reverse T3: 18.4 ng/dL (reference range: 9.2-24.1)

Convert pg/mL to ng/dL: multiply by 100—3.1 x 100 = 310

310/18.4 = **16.8**

With a ratio of 16.8 (low) it is even more important to treat sources of increased oxidative stress in the body when **reverse T3 is very high** and **T3 levels are still normal** (as above) than to just give dessicated thyroid and/or T3. Often, at first, both approaches are indicated. Follow-up is important for long-term clinical fine-tuning.

## Magnesium Supplementation

**Magnesium**:

Many oral forms exist, and vary widely in absorption and bioavailability. Good forms include chloride, glycinate, gluconate, and threonate.

Whenever possible, include magnesium (usually as sulfate) in an intravenous infusion for any clinical reason.

Highly effective: liposome-encapsulated magnesium threonate

Transdermal applications can further improve magnesium status.

Nebulization (magnesium chloride) can be enormously beneficial, especially in conjunction with DMSO, sodium ascorbate, and insulin. This can penetrate biofilms, kill pathogens, and normalize oropharyngeal flora, and gut health can improve dramatically as pathogens are no longer swallowed "24/7."

## Optimizing IOS, VC, and Mg status

Nebulization:

DMSO, MgCl, sodium ascorbate, and insulin mist inhalations appear to normalize nasopharyngeal flora, minimizing the chronic swallowing/ingestion of pathogens and pathogen-related toxins. Anecdotally, gut function appears to rapidly improve as well.

Many other agents and combinations can be used, including hydrogen peroxide, zinc, colloidal silver, sodium bicarbonate, N-acetyl cysteine, and nascent iodine. As long as an agent is well-tolerated during the nebulization procedure and does not make it more difficult to breathe freely, there appears to be no significant downside.

## Increased IOS and the Eye

Antioxidant carotenoids, such as lutein, astaxanthin, and zeaxanthin, along with vitamin E, have long been recognized and documented to be critical in minimizing oxidative stress in the eye and its related structures. However, the role of vitamin C in the eye, as throughout the rest of the body, still makes it the antioxidant of primary interest, as it is essential for keeping ("recharging") these other antioxidants in their protective, reduced state [21296184]

As vitamin C protects all of the cells and tissues in the body in a similar fashion, it has been established that maintaining higher blood levels of vitamin C results in greater longevity, with a clear reduction in death from any cause (all-cause mortality) [8694019, 10817122, 11247548, 11444422, 22237767, 25315508, 25948669, 28574431, 30239557, 29806637]

## Increased IOS and the Eye

IOS is massively increased in the cells involved in proliferative diabetic retinopathy (10-fold decrease in the levels of vitamin C in the vitreous humor). Furthermore, the degree of macular ischemia has been directly correlated with the degree of vitamin C depletion (along with other critical antioxidants) [31216331]. The retina is one of the highest oxygen-consuming tissues in the body, resulting in an especially large generation of reactive oxygen species (increased oxidative stress) [22510306]

Regular supplementation with vitamin C and/or different carotenoids resulted in a reduced complication rate and improved visual acuity scores [31100179, 22009916]

## Increased IOS and the Eye

Antioxidant deficiencies, especially of vitamin C, are characteristic of commonly studied eye disorders and diseases. Furthermore, maintaining **higher intakes** of vitamin C (optimally through supplementation) **reduces the incidence** of ocular diseases, such as cataract, glaucoma, and age-related macular degeneration [18421094, 21705085, 28933356]

## Increased IOS and the Eye

**Diabetic retinopathy and macular degeneration**

Prototypical disease for **intracellular scurvy**, with extremely and **chronically** elevated IOS in the cytoplasm of the affected ocular cells/tissues

Insulin promotes the cellular uptake of both glucose and vitamin C uptake via the same transmembrane transporters.

Therefore, the more circulating glucose, the less vitamin C gets inside the cells (competitive inhibition) [6547412, 9550452]

## Increased IOS and the Eye

**Glaucoma and cataracts**

Normal-tension glaucoma patients have lower serum levels of vitamin C than normal, healthy controls [19763599] There also appears to be a greater risk of "regular" glaucoma in patients with lower vitamin C levels [22171153, 29104244]

Generally, vitamin C content in the aqueous humor declines with age, but judicious supplementation can counter this decline. Also, lower levels of vitamin C intake further augments the ability of a cataract-forming agent (ultraviolet radiation) to exert its effect [22155581]

## Increased IOS and the Eye

**Glaucoma and cataracts**

Supplement well, but also consider delivering antioxidant capacity as directly to the eye as possible [24187660, 25643848]

Anecdotal evidence supports the benefit of eyedrops containing 1.25% glutathione, 1.25% vitamin C, and 6.25% DMSO, appropriately compounded and pH-balanced in retarding early cataract formation.

Perhaps the addition of magnesium chloride in the solution would offer substantial further benefit? (Optimize intracellular oxidative stress with optimal magnesium and vitamin C levels…)

## Multi-C Protocol, Current

1. Oral liposome-encapsulated vitamin C (for optimal ***intracellular*** access by ascorbate, as well as in subcellular organelles)
2. Multigram doses of sodium ascorbate powder, taken several times daily, up to or reaching bowel tolerance (in order to minimize gut toxicity & support ***extracellular*** access by ascorbate) [7321921, 4069036]
3. Oral administration of ascorbyl palmitate (for optimal ***fat-soluble*** access by ascorbate) [15209539, 12595755, 9890643]
4. Intermittent IV administration of ascorbate (to optimize ***extracellular*** access by ascorbate, as well as to further ***support*** intracellular pools of ascorbate); also **IV push applications**, sometimes with insulin and/or hydrocortisone and/or magnesium; continuous low-dose infusion (Riordan Clinic)
5. Intramuscular administration of ascorbate
6. Agents that promote and sustain vitamin C in the plasma (reversal of acquired epigenetic deficiency)

## Multi-C Protocol Endogenous VC production

Many sailors have survived the scurvy that has slain many others.

Fetuses produce large amounts of vitamin C [4830116]

Breastfed babies often continue to make large amounts of vitamin C [6496385]

Some guinea pigs and human adults continue to spill vitamin C long after being subjected to otherwise scurvy-producing degrees of vitamin C deficiency and depletion [5231398, 5116040, 4550033, 7211730, 5497811, 1032629]

## Increased IOS and the Eye

**Corneal health**

Quality, scar-free healing in corneal wounds can be problematic.

Vitamin C in topical gels has been shown to support good corneal healing with enhanced tissue matrix regeneration while maintaining optimal transparency [29128534] Animal studies have supported this ability [28276172, 22832865]

## Multi-C Protocol Endogenous VC production

A nutrient polyphenol supplement now available consistently “unblocks” the genetic defect that otherwise blocks the human liver from synthesizing vitamin C [28063380]

The genetic defect involved is epigenetic in nature, not a genetic one. It comes from defective transcription by the ribosome, not from a flawed genetic (DNA) sequence. While the precise mechanism remains to be delineated, this nutrient appears to permit transcription that is typically blocked by abnormally placed “stop codons.” [29131862]

## Multi-C Protocol Endogenous VC production

It also appears that the restoration of this VC-synthesizing ability permits the reflex synthesis and release into the blood of much larger amounts of VC when significant toxic (oxidative) exposures occur. Rather than see VC levels drop to zero in the urine, they increase and remain increased until the increased oxidative stress has been adequately neutralized.

## Multi-C Protocol
## Endogenous VC production

An additional extremely important aspect of this restoration of VC synthesis in humans comes from the fact that the liver uses glucose as the natural substrate to make the vitamin C.

This is the perfect natural design: Use up otherwise damaging excess glucose while forming the most important nutrient in the body.

Animals in the wild are not injecting themselves with insulin several times a day…

## Recap

1. Increased intracellular oxidative stress (IOS) is the pathology common to all diseases and medical conditions.
2. When enough vitamin C gets inside the cells (along with increased Mg and decreased Ca), increased IOS no longer exists.
3. There are multiple ways to optimize intracellular VC (Multi-C Protocol)
4. Optimal magnesium and calcium metabolism, along with a balancing of sex hormones and thyroid, is essential for normal IOS and an optimal clinical status for all diseases, including ocular diseases.

## Multi-C Protocol
## Endogenous VC production

Additional vitamin C supplementation is still desirable even when the ability to synthesize vitamin C has been restored, especially when considering the best ways to prevent new infections and to promote the resolution of chronic diseases.

The liver "responds" to increased oxidative stress, but it cannot anticipate it. So, a high viral exposure will still result in causing a col or flu. Higher vitamin C dosing on a regular basis is still necessary to optimally prevent contracting such diseases.

## For Contact and Further Information

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