Microscopic Colitis Foundation

Newsletter Archive

Wayne's Blog

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The Future of IBD Treatment — and Where MC Fits In

by Wayne Persky

Here's an honest view of what the promising new therapies that are transforming the treatment of CD and UC might mean for MC patients.

IBD treatment is changing faster than at any point in the disease's modern clinical history. A new generation of targeted therapies, including JAK inhibitors, selective biologics, microbiome-based interventions, and combination approaches, is producing remission rates in Crohn's disease (CD) and ulcerative colitis (UC) that would have seemed unreachable a decade ago. For MC patients watching this progress, the natural question is — “when does any of this reach us?”

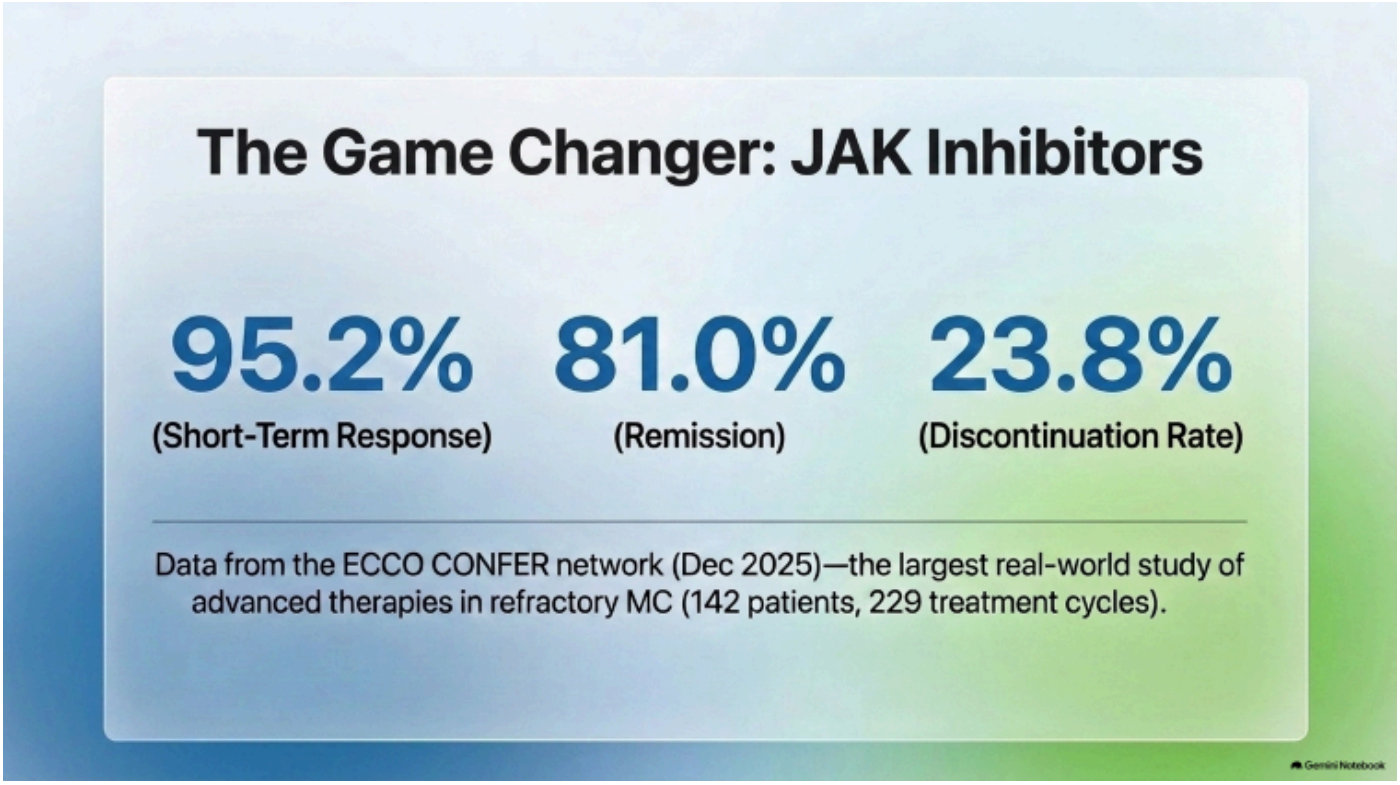
The honest answer, as it so often is for our community, is complicated. MC has long been the neglected member of the IBD family — well-studied enough to be recognized, not well-studied enough to have its own robust treatment options. Most of what we know about treating refractory MC comes from extrapolating CD and UC research, and hoping the findings might translate. Sometimes they do. Sometimes the evidence, when it finally arrives, is more complex than the extrapolation suggested.

This article attempts to give MC patients an accurate picture of where IBD treatment is heading, what the emerging therapies actually are, and most importantly, what evidence exists specifically in MC rather than just in the broader IBD category. Those are different questions, and attempting to blend them has misled our community before.

Why has MC lagged behind CD and UC in treatment development?

The disparity in the number of research studies between MC and the other IBDs is not accidental. Clinical trial funding, whether from industry or government, flows toward diseases with large, well-characterized patient populations, clear diagnostic endpoints, and established drug marketing opportunities. CD and UC have all three. MC has a larger patient population than most physicians realize, but it has historically been underdiagnosed, underreported, and understudied. And pharmaceutical companies have little incentive to run expensive randomized controlled trials for a disease, when off-label use of existing drugs provides an accessible alternative treatment.

The result is minimal treatment offerings in which budesonide (a corticosteroid first approved for MC in Europe in the early 2000s), remains the only medication with strong, MC-specific randomized controlled trial evidence. Everything beyond budesonide is borrowed from other diseases and applied to MC through clinical judgment, small case series, and retrospective cohort studies. That's better than nothing, as those studies have genuinely expanded our options, but it means that the evidence base for second- and third-line MC treatment is considerably smaller than most patients, and many physicians. would prefer.



JAK inhibitors are the most promising development for refractory MC.

Janus kinase (JAK) inhibitors, a class of small-molecule drugs that block intracellular inflammatory signaling pathways, have shown impressive results in treating UC, and are increasingly being used to treat CD. Three are currently approved for UC in the United States: tofacitinib (Xeljanz), filgotinib (Jyseleca), and upadacitinib (Rinvoq), with upadacitinib showing the strongest efficacy data in head-to-head comparisons (Ananthakrishnan et al., 2024)[1].

For MC specifically, the most significant recent evidence comes from the ECCO CONFER network (a multinational European IBD research collaboration), which published the largest real-world study of advanced therapies in MC to date, in December 2025. Among 229 treatment cycles in 142 budesonide-refractory MC patients, JAK inhibitors produced the highest short-term clinical response rate of any treatment class studied — 95.2% response and 81.0% remission. Long-term drug persistence was also

markedly better for JAK inhibitors than for anti-TNF agents or vedolizumab, with a discontinuation rate of only 23.8%, compared to 56.3% for other treatments (Verstockt et al., 2026)[2].

These are impressive numbers, and the authors of the ECCO CONFER study were themselves struck by them, describing JAK inhibitors as a potentially transformative treatment option for refractory MC, while immediately and appropriately calling for rigorous clinical trials to confirm what retrospective real-world data can only suggest. The sample sizes for JAK inhibitor use in MC remain small. The ECCO CONFER cohort included only 21 JAK inhibitor treatment cycles, and safety data specific to MC patients on these drugs is limited. JAK inhibitors carry known risks, including increased susceptibility to serious infections, reactivation of herpes zoster, and a cardiovascular risk that prompted the U.S Food & Drug Administration (FDA) to add a black box warning in 2021 (U.S Food & Drug Administration, 2021, December)[3]. For older MC patients, who make up the majority of cases, those risks require careful individual assessment.

Anti-TNF agents are effective, but have a high rate of loss-of-response.

Anti-tumor necrosis factor (Anti-TNF) biologics, infliximab (Remicade) and adalimumab (Humira), were the first advanced therapies used for off-label treatment of MC patients who were refractory to budesonide, and they remain the most commonly used. In the ECCO CONFER study, anti-TNF agents were initially used in 55.9% of treatment cycles, making them by far the most frequently prescribed advanced therapy for refractory MC.2 Short-term response rates are reasonable, but long-term persistence is poor. More than half of patients eventually discontinued anti-TNF therapy because of lack of response, loss of response, or adverse effects. That pattern mirrors what has been observed in CD and UC, where anti-TNF agents are effective in a substantial proportion of patients, but are associated with significant rates of secondary failure over time.

Vedolizumab is a gut-selective option with a favorable safety profile.

Vedolizumab (Entyvio) is a biologic that specifically targets gut lymphocyte trafficking rather than systemic immune pathways, which gives it an advantageous safety profile compared to anti-TNF agents, which is particularly relevant for older MC patients who have comorbidities that increase infection risk. In the ECCO CONFER study, vedolizumab accounted for 28.8% of treatment cycles, and showed reasonable efficacy, though lower than JAK inhibitors. Its safety profile makes it a particularly attractive option for patients who cannot tolerate the systemic immunosuppression associated with anti-TNF agents or JAK inhibitors European MC guidelines have specifically noted vedolizumab's safety advantages for older patients with comorbidities as a reason to consider it even when other options might show numerically higher remission rates (Miehlke et al., 2021)[4].

Ustekinumab and emerging biologics:

Ustekinumab (Stelara), an anti-IL-12/23 biologic, has shown efficacy in both CD and UC and has been used off-label in refractory MC, though the evidence base in MC is particularly thin, with individual case reports and small series rather than even the modest cohort data available for vedolizumab and anti-TNF agents. The ECCO CONFER study included only a handful of ustekinumab cases, insufficient to draw meaningful conclusions.[2] Note that ustekinumab has been approved by the FDA for pediatric IBD use.

Newer anti-IL-23 biologics, risankizumab (Skyrizi) and mirikizumab (Omvoh), have shown impressive efficacy in UC and CD, with risankizumab ranking among the highest-efficacy options in a 2024 AGA evidence synthesis for UC.1 A synthesis takes information from multiple sources, compares them, and combines them to create a completely new, unified understanding. No meaningful MC-specific data exists for these agents yet, though the shared inflammatory pathways between MC and UC make them possible candidates for off-label investigation as the drugs become more widely available.

Dual pharmacological therapy shows promise, but there are some serious unanswered questions.

One of the more intriguing recent developments in IBD treatment is dual-targeted therapy — combining two biologic agents, or a biologic with a JAK inhibitor, to simultaneously block multiple inflammatory pathways in patients with refractory disease. A 2025 review in Biomolecules documented growing evidence

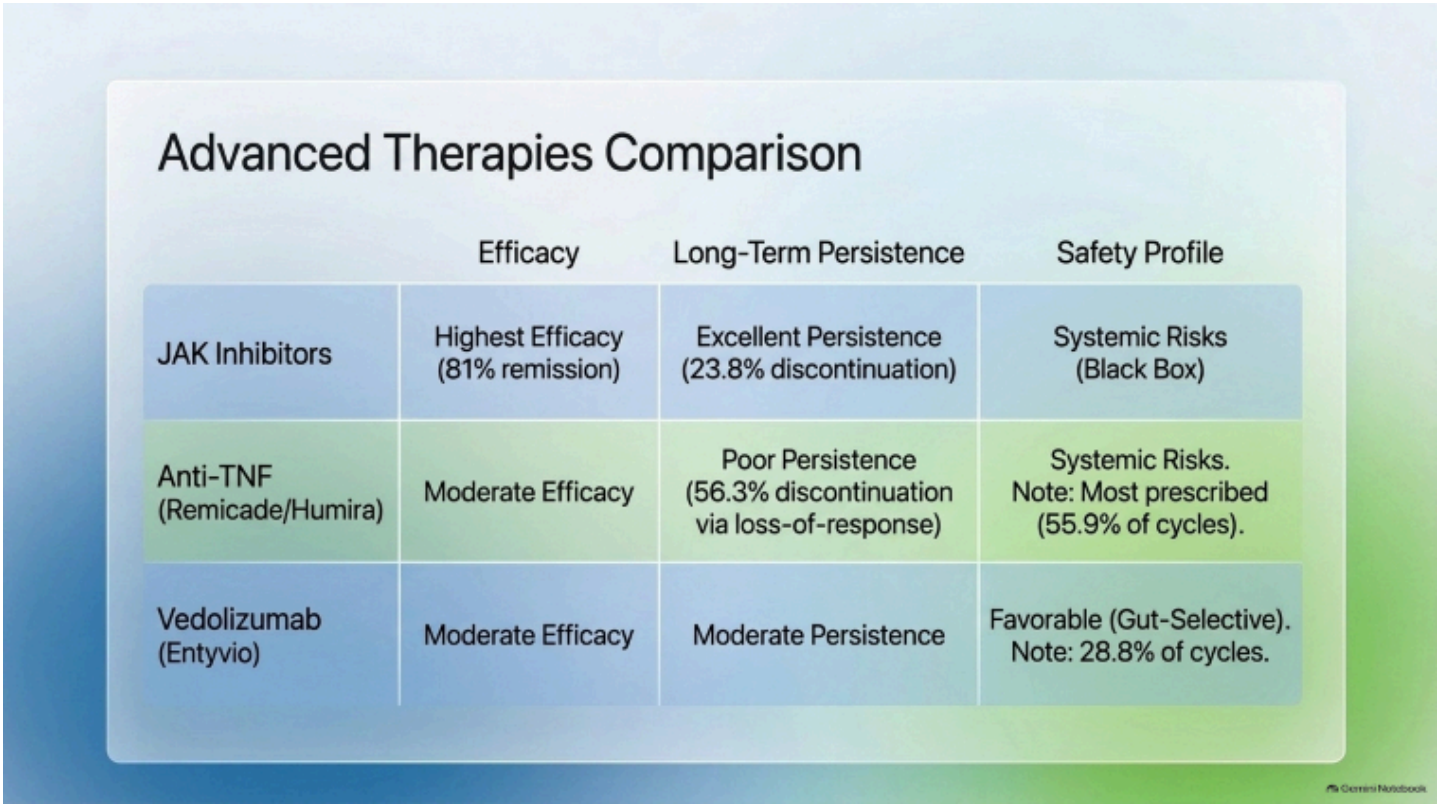
that dual therapy can improve clinical and endoscopic outcomes in patients with CD and UC who have failed multiple single-agent approaches (Altieri et al., 2025).[5]

For MC patients, this remains largely theoretical, because there's no published dual therapy data for MC. But it represents a possible future option that severely refractory MC patients may eventually choose to consider, as the approach becomes better established for IBD in general. Before that happens, however, the safety considerations deserve more honest discussion than the current IBD literature usually provides.

Combining two powerful immunosuppressive agents doesn't simply add their individual risks together — it may multiply them. Each of the drug classes used in IBD carries its own serious adverse event profile. For example, anti-TNF agents increase the risk of serious bacterial infections, reactivation of tuberculosis and hepatitis B, and certain malignancies. JAK inhibitors carry additional risks of herpes zoster reactivation, cardiovascular events, and blood clots. The newer IL-23 biologics have shorter track records with limited long-term safety data.

When two of these agents are used simultaneously, they suppress the immune system through different but overlapping pathways, and the long-term consequences of that combined immunosuppression are not yet well understood. The Biomolecules review acknowledged that safety data from dual therapy studies have so far appeared broadly consistent with monotherapy profiles, but the trials conducted to date have been too small and too short to detect rarer but serious adverse events that might emerge over years of treatment

For older MC patients, already the group most vulnerable to infection and cardiovascular risk, this is an important consideration, not just a footnote.



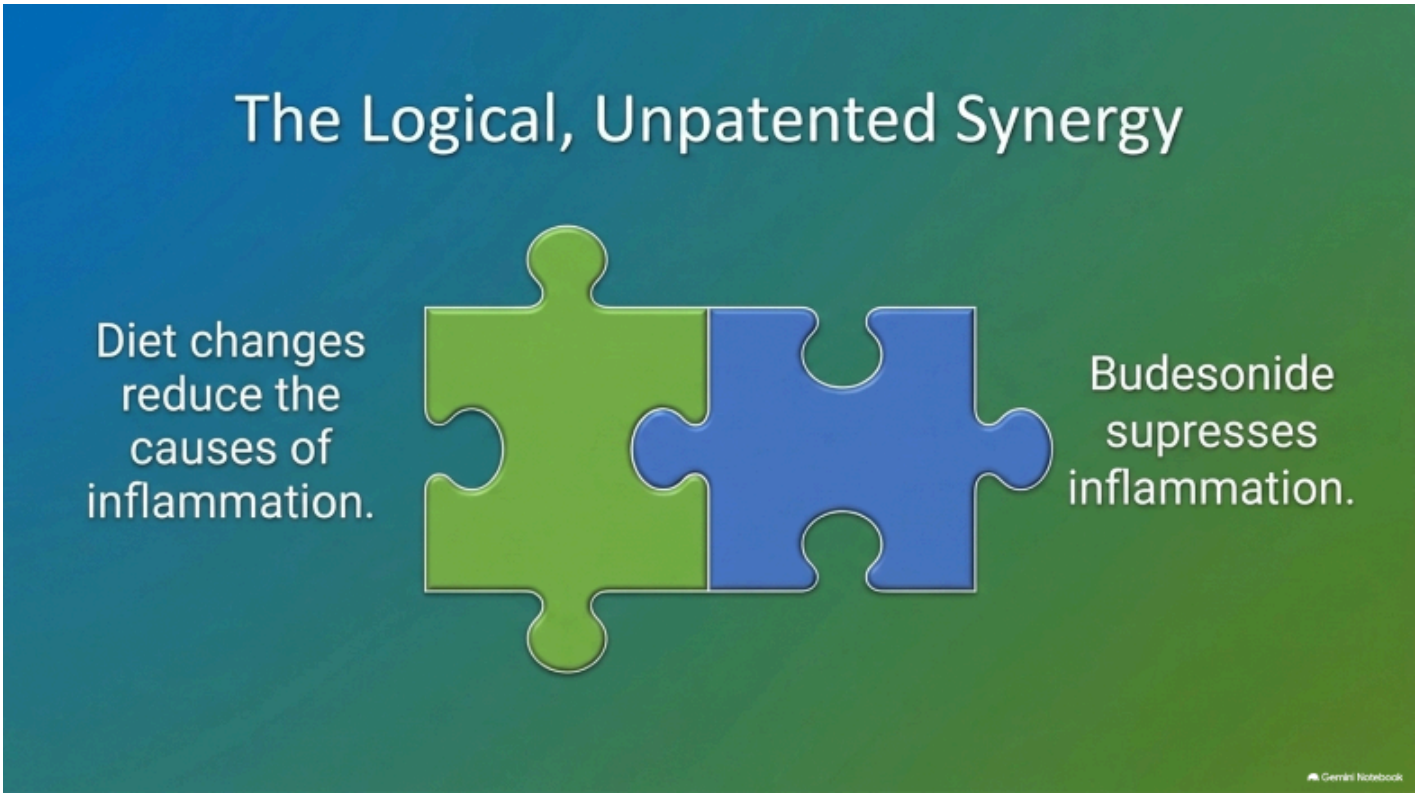
The combination approach researchers aren't studying, but should be:

The dual therapy discussion in the IBD literature shares a blind spot that runs through most IBD pharmacological research — it considers only combinations of drugs. The possibility of combining medication with the dietary modifications that real-world MC patients have found effective, and which many of us are already using successfully, receives virtually no attention in the clinical trial literature.

This is not because the idea lacks scientific merit. It's because dietary interventions can't be patented. A pharmaceutical company can fund a trial of biologic A combined with biologic B because, if the

combination proves superior, both drugs can be marketed at premium prices. Nobody can patent a gluten-free, dairy-free, soy-free diet combined with budesonide; which means that nobody with the resources to run a large clinical trial has a financial incentive to study it. The result is that one of the most logical and potentially safest combination approaches — properly structured diet changes to reduce the inflammation level so that a medical treatment such as budesonide is more likely to bring remission, isn't even on researcher's radar, — not because it doesn't work, but because the research funding system offers no rewards for studying it.

The practical experience of the MC community suggests that dietary management and medication work better together than either does alone for many patients. Members of the Microscopic Colitis Foundation forum have consistently reported that budesonide is more effective, and remission more durable, when dietary triggers are systematically eliminated at the same time. That observation is consistent with what the biology would predict — reducing the antigenic load on an inflamed mucosa while simultaneously suppressing the immune response addresses the problem from two directions at once, just as dual pharmacological therapy aims to do, but without stacking the adverse event profiles of two powerful immunosuppressive drugs. A well-designed clinical trial comparing budesonide alone versus budesonide plus structured dietary elimination in newly diagnosed MC patients would be relatively inexpensive compared to pharmaceutical trials, and potentially highly informative. The fact that no such trial exists says more about research funding priorities than about the question's scientific merit.



What about fecal microbiota transplantation?

Fecal microbiota transplantation (FMT), although promising in principle, remains limited in MC-specific evidence, despite the fact that it has been around for many years.

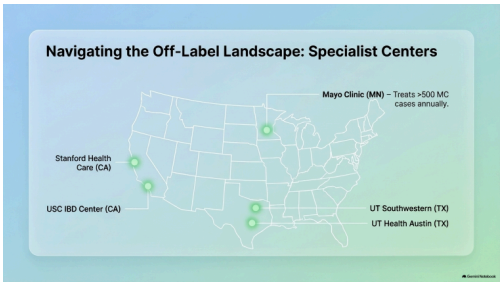
FMT) involves transferring gut bacteria from a healthy donor to a patient with dysbiosis. The procedure has produced remarkable results when used for treating recurrent Clostridioides difficile infections, and there's moderate evidence of benefit in UC. The theoretical rationale for FMT in MC appears at first glance to be sound, since MC is associated with gut microbiome disruption, and restoring a healthier microbial balance could theoretically reduce mucosal immune activation. But in practice, the needed MC-specific evidence for FMT is almost nonexistent. Individual case reports exist, but no controlled trials have been published. FMT remains experimental for MC and is not currently a realistic option outside of research settings.

But if we look at this situation realistically, there doesn't appear to be a significant reason why FMT should bring anything more than a brief beneficial effect. Dysbiosis is not a known primary cause of MC. Dysbiosis is a result of the compromised digestion, and the malabsorption problem associated with MC that allows opportunistic bacteria to become established in the gut, and dominate the microbiome. It's known to be associated with MC, but definitely not known to cause MC. In other words, dyabiosis is a side effect of MC, not a primary cause of MC, so it shouldn't be surprising that FMT wouldn't be an effective treatment.

What the research gap means for MC patients right now:

The practical implication of everything described above is that MC patients with budesonide-refractory disease have more options than they did five years ago, but are still navigating those options largely without the kind of robust, disease-specific evidence that UC and CD patients can utilize. The ECCO CONFER study is the most encouraging development in refractory MC treatment in recent years, and its JAK inhibitor findings in particular suggest that at least some MC patients who have cycled through budesonide without achieving remission may respond well to a class of drugs that remains dramatically underused in our disease. But the authors of that study themselves are clear: the era of small case series and anecdotal evidence must give way to rigorous clinical trials, and those trials have not yet been conducted.

For MC patients who don't respond to budesonide, and haven't yet had a conversation with their gastroenterologist about advanced therapies, that conversation is worth initiating. The European MC guidelines already recommend referral to an IBD center with advanced therapy experience for severe or refractory cases.4 Most general gastroenterologists have limited experience with JAK inhibitors or biologics in MC specifically, because the volume of MC patients requiring advanced therapy in any single practice is so small, and centers that see large numbers of IBD patients are better positioned to make informed decisions about which agent to try and in what sequence.



Do such centers of IBD treatment excellence exist in the U.S.?

There are many, for CD and UC. For MC patients who have difficult or treatment-resistant cases, some of the best choices include:

1. Mayo Clinic — Rochester, Minnesota — strongest overall MC expertise; treats >500 MC patients annually and specifically treats patients who fail standard therapy.
2. Stanford Health Care IBD Program — Stanford, California — explicitly treats microscopic and collagenous colitis, including complex/refractory disease.
3. UT Southwestern Crohn's & Colitis Program — Dallas, Texas — explicitly treats microscopic, collagenous and lymphocytic colitis.
4. UT Health Austin IBD Clinic — Austin, Texas — explicitly reports extensive MC experience and access to newer therapies.
5. USC IBD Center — Los Angeles, California — specialized IBD center that explicitly includes microscopic colitis.

The larger picture is one of cautious optimism qualified by an honest acknowledgment of how far behind the research is. IBD treatment is genuinely improving, and some of those improvements are beginning to reach MC patients through off-label use and the growing body of real-world evidence. The gap between what's available for CD and UC patients, and what's available for us is narrowing, although still very unsatisfactory. What we're still waiting for, and what our community should continue to advocate for, is the kind of dedicated MC research that would tell us definitively which treatments work, for which patients, and in what sequence. Until that research exists, we're still extrapolating.

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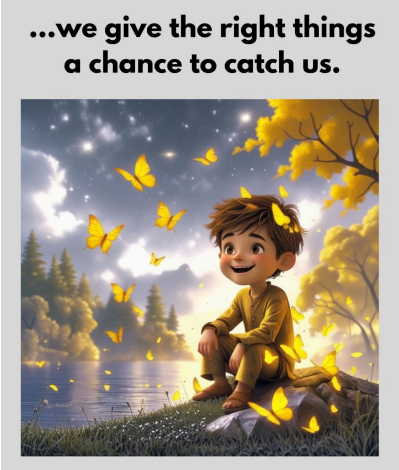
In Honor of Fall: Be Like the Leaves ~ Let Go

by Shannon Freedom

There is something deeply freeing about letting go of what has been feeling heavy. It can be an expectation, a fear, a resentment, a relationship, a thought, or simply something that has outgrown its place in our lives.



When we release what we no longer need to carry, we may feel an unexpected wave of relief. We may feel lighter, more grateful, peaceful, joyful, and even a renewed sense of aliveness. We may feel more spacious within ourselves, as though energy that was once devoted to holding on has become available for simply being.

Sometimes letting go can even bring tears. Not necessarily from sadness, but from the profound release of finally allowing ourselves to put something down. There can be a sense of returning to ourselves, reconnecting with what matters, and realizing that we do not have to carry everything simply because we have carried it for a long time.

How do we drop the heavy negativity?

By dropping it. How do you drop a hot piece of coal from your hand? Or some heavy and useless baggage? By recognizing that you don't want to carry the burden or suffer the pain any longer, and letting it go.

Mental mantras and visualizations may also aid in the process of letting go. Any time during the day when we begin to notice ourselves getting stirred up, we can also repeat "let go" until it fizzles out. Imagery can also be useful to help us feel as though weight is literally falling off our shoulders. Sometimes, simply visualizing ourselves releasing what we've been carrying can create a sense of lightness.

A big part of letting go is feeling safe enough to release what we've been holding onto and trust what comes next.

Things often fall into place when you stop pulling the strings, relax, and allow life to guide you. After all, panic has never solved anything. Both fear and faith that all will be okay ask you to believe in something you cannot see. The choice is yours.

Meditation can be used to strengthen our connection to our inner wisdom for guidance. In my experience, I've noticed more things falling into place when I meditate. Epiphanies happen. Moments of *"I was just*

thinking that!" or *"I was just about to text you too!"* exponentially increase. There is great power in the present moment, when we are not replaying the past or worrying about the future.

And who knows, maybe as we learn to let go mentally, the body will begin to let go physically, too. Maybe the gut will learn to let go of what it has been holding on to for too long. Maybe any muscle tension contributing to headaches, joint pain, fatigue, or unideal postures (especially those affecting digestion) will begin to release as well.

Of course, letting go takes momentum, and it takes time. Like a wheel that has been spinning and is beginning to slow down, it will continue moving for a little while before eventually fizzling out.
Trust the process.
Once we are reminded of what mental peace feels like, we don't want to forget it. And once we've experienced that peace, holding on to the silly little things that once consumed us may no longer feel worth it.

Like the leaves of autumn, we can trust that releasing what is no longer serving us does not mean we are losing ourselves. Sometimes, it is what allows us to save energy and make room to receive healing, new growth, and a healthier way of living.

A great time to practice letting go is at the end of the day. Allow an 30-60 minutes before bed to let it all go and wind down. Think of it like closing all the open tabs on a computer. Close them out. Trust the process. Close your eyes.

Let It Go.

Check Out Wayne's Blog

He posts a new blog about once a week. Here are the titles of the most recent. Click the button at the top of the newsletter to access.

Pregnancy and Microscopic Colitis — Why Hormonal Changes Help Some Women and Harm Others

MC Causes Brain Fog by Disrupting Our Sleep

Can a Routine Colonoscopy Cause Microscopic Colitis?

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