Migraine Prevention: Finding the Right Therapy

Even working with a medical provider you trust, the process of finding an effective migraine prevention treatment can be frustrating. What you want is a treatment that will significantly reduce your headache burden, will do so within a relatively short time of beginning the treatment and will not cause a bundle of side effects worse than the migraine it's intended to treat. With all the treatments now available, why is it so difficult and time-consuming for medical providers to identify a migraine prevention treatment that meets the needs of the individual patient? To provide a meaningful answer to that vexing question it may help to take a brief detour.

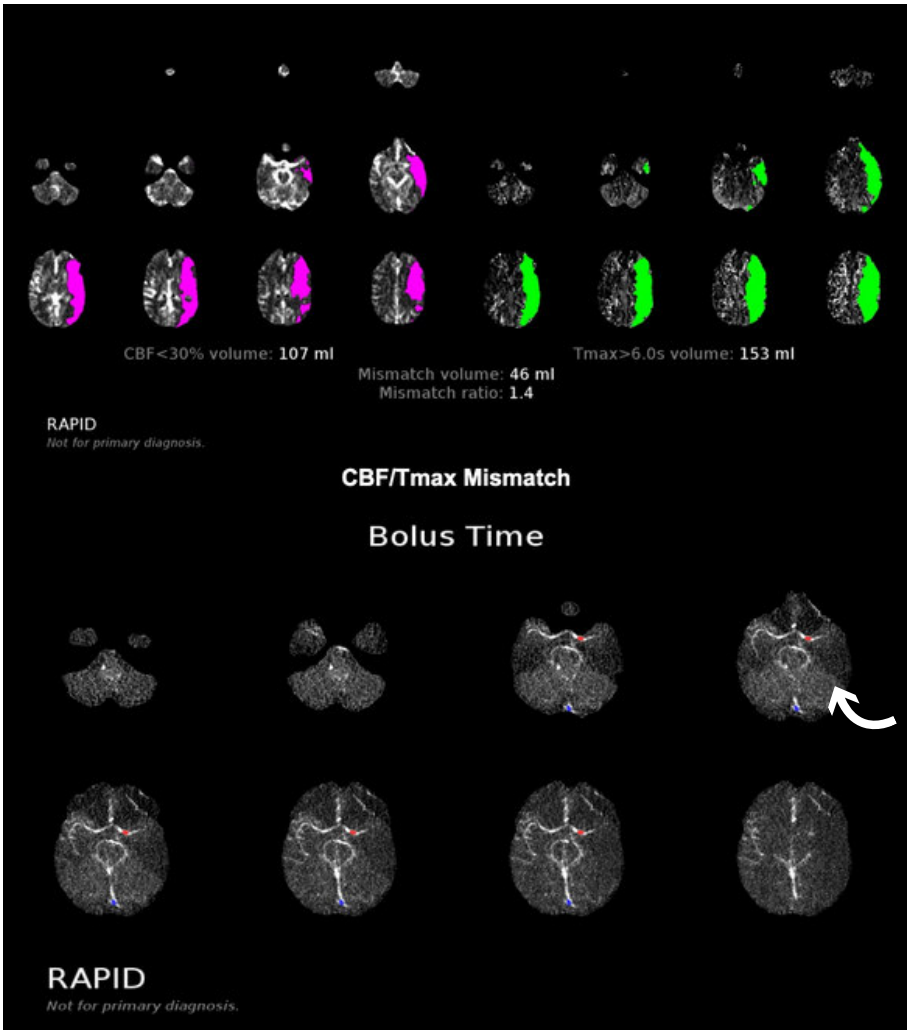
While migraine is the most common neurologic disorder that leads one to seek medical attention, stroke is the most common neurologic disorder to require hospitalization. Each year about 800,000 Americans suffer an acute stroke, and about 80% of those strokes are *ischemic* (with an ischemic stroke, a blood vessel supplying the brain is obstructed by clot, and the area of brain supplied by that vessel consequently dies; with *hemorrhagic* stroke, a blood vessel ruptures and spills blood into the area around it).

Despite its prevalence, until 1996 there was no FDA-approved therapy for the treatment of acute ischemic stroke. At that point intravenously administered tissue plasminogen activator (TPA), a protein that dissolves blood clots, became available for general clinical use.

If a patient presented to emergency room with symptoms and signs suggesting acute stroke (for example, inability to move the left arm and leg), a brain CT scan demonstrated no evidence of bleeding within the brain and there was no other contraindication to treatment, intravenous TPA was administered.

If the paralysis of the left arm and leg reversed, it was assumed that the brain tissue rendered unable to function by the loss of blood supply had not yet died and now had resumed functioning due to TPA having dissolved the obstructing clot and restored blood flow. If the paralysis persisted unchanged despite restoration of blood flow, then it was assumed the brain tissue was dead by the time the TPA was administered. Before the fact, there was no way to accurately predict who would or would not benefit from TPA.

How things have changed: when the author of this article is on call for stroke, he receives a text message that provides precisely the information included in the example ("Acute Stroke") provided below. This particular patient has suffered an acute stroke involving the left hemisphere of the brain. The green areas in the CT-derived images on the right demonstrate what portion of the brain is not receiving an adequate supply of blood. The dark pink areas in the images on the left demonstrate how much of the brain within the green area is irreversibly damaged. The images below these scans demonstrate the major blood vessels within the brain, and in this case a major



artery supplying the left hemisphere is blocked by clot. A computer calculates the ratio of brain volume deprived of blood compared to brain volume irreversibly damaged, and if that ratio is favorable the patient immediately goes for arteriography to confirm the artery is indeed blocked and then mechanical thrombectomy to restore flow (the thrombectomy involves insertion of a clot retrieval device located at the end of a long catheter that is inserted in a groin artery and threaded up to the brain). To someone who has been involved in stroke and stroke research for many decades, this seems to me nothing short of miraculous. Contrast this vast technological leap to our use of therapies for stroke prevention. While the medical provider may obtain a brain imaging study or other diagnostic tests to exclude conditions mimicking migraine, the diagnosis of migraine ultimately lies in the history provided by the patient. Unfortunately, there often is little in that history to guide the choice of a prevention therapy. If the patient has truly tried and failed a given therapy in the past, then it makes little sense to walk down that same path once again. Certain therapies (e.g., onabotulinum toxinA/BotoxA) have been proven to be effective for **chronic migraine**, but not episodic migraine; others (e.g., certain beta-blockers/ propranolol, timolol) are effective for episodic migraine but have no solid evidence of benefit in treating chronic migraine; and yet others (e.g., **the anti-CGRP Mabs**) are known to be effective for prevention therapy in both varieties of migraine.

Beyond this, there is little in the patients' histories that will assist a provider in selecting the "correct" prevention therapy, and there exists no diagnostic test or biologic marker that will indicate whether a given prevention treatment is more or less likely to succeed. Thus migraine prevention therapy remains a process of "educated trial and error". It is the responsibility of the provider to carefully take into account the patient's headache burden, the patient's previous experience with prevention therapies, the presence or absence of any coexisting disorders (e.g.s, high blood pressure, depression, chronically disrupted sleep), co-existing medications, pregnancy issues and a variety of other less tangible variables to select for the individual patient those options which seem to be the best "fit".

On the other side of the therapeutic alliance, it is the patient's responsibility to provide the best history he or she can, to comply with the therapy prescribed and promptly to report to the provider any side effects or other problems that make it difficult or impossible to comply.

As with ischemic stroke, the day will come when we will have far more sophisticated tools for guiding migraine prevention therapy. It's not inconceivable that "gene editing" from a simple blood specimen will enable providers to select therapies that fit" the individual patient biologically as well as clinically, and the day may come when gene editing will permit modification of the manner in which the patient's "migraine providers to select therapies that fit" the individual patient biologically as well as clinically, and the day may come when gene editing will permit modification of the manner in which the patient's "migraine.