FINDING THE RIGHT MEDICATION

OR

(Why our zebra stripes have different patterns)

Drug tolerance or failure for a drug to continue to work is a common problem with long-term pharmaceutical therapies. Every system is wired differently and the drugs behave differently based on that wiring.

Biologic drugs (such as Rituxan/Rituximab) impact an immune system which has become overactive, sending signals to attack native cells. Biologics block the activity of specific substances: TNF (tumor necrosis factor), IL-6 (interleukin-6), IL-1 (interleukin-1), or two types of white blood cells (B-cells and T-cells).

If you take a drug that blocks TNF for a while, the body can figure a way around it and continue its attack. The immune system is very determined, even when it is wrong. Conversely, the body may see the drug as an enemy and build antibodies against the drug. The patient then must try a different drug.

They are working on blood tests to determine which patient will respond to which biologic or disease-modifying drug, but we are not there yet.*

Pain medications (opioids such as Tramadol, Oxycodone, Vicodin, etc.) and muscle relaxers (such as Valium, Baclofen, Xanax) work by attaching to specific receptors in the brain to keep cells from communicating.

A basic sketch of the nervous system consists of neurons with plugs at one end and receptors at the other. One end (the cell body) has dendrites (receptors) that absorb chemical signals. The signals have to be very strong or repetitive to make it past the axon hillock (the spam filter). Once the spam filter decides a message is important enough, out of millions of signals (excitatory or inhibitory) per second, it is sent down the axon cable to the axon terminal that releases neurotransmitters which will cross the synaptic cleft to the dendrites (receptors) of the next neuron. Axon cables have many different lengths.

As a simplified example there are two main categories of signals: go (such as glutamate) and stop (such as GABA). There are signals that tell the organs to produce hormones and other signals that tell the organ to cut it off.

The excitatory system can hijack the inhibitory system messages at any point along the line and vice-versa. The neuron's preferred state is at rest. The excitatory signals come along and make it do something. The system breaks down when the balance between excitation and resting become imbalanced.

With drug exposure, over time, several things can go wrong. The receptor can actually be absorbed by the cell, so the drug signal no longer has a receptor. This is called down-regulating and happens because cells try to protect themselves from repeated exposure to foreign chemicals. *

Also the number of excitatory signals can increase, requiring more inhibition of the signals. Therefore the body requires higher doses to get the message across.

Opioid rotation (switching meds) may be necessary when this happens. Each patient's reaction to a drug is different than someone else's because their neural network is inherently different.

With opioids, a study revealed that by slowly tapering the dose, pain levels paradoxically go down in some patients, as does depression.*

To understand why one patient responds and another doesn't, you have to look to the person's DNA, environmental exposures, the level of signals (neurotransmitters and hormones) produced, the ability of the cells to receive the signals, the number of receptors, and the areas where the signals get interrupted.

Maybe someday we'll have a computer that can scan the neuroendocrine network and find the places where the intricate system is broken.

Some patients respond well to a treatment for a long time. Some respond initially but the effect wears off. Some don't respond at all. For now it is a matter of trial and error. *(*referencing an article in Arthritis Today*).