SOARING Rx

BY DR. DANIEL L. JOHNSON

The Tumescent Personality

To know yet think that one does not know is best; not to know yet to think that one knows will lead to difficulty. – Lao Tzu

Caution: Reader discretion advised regarding adult content, biological details, and pharmacology.

Oscar turned into a bump, lost it, banked more steeply, and in a quarter-turn got it back again, then lost it just as quickly. He'd been scratching around for an hour on this windy blue day, hoping to get enough altitude to get away, hoping to find enough organized lift to stay away. He was getting tired and feeling pessimistic. It was hard to get up and hard to stay up. Maybe today's flight would be a local one.

Oscar was getting older, on the cusp of retirement. Was this how he wanted to spend his soon-to-be-abundant free time? As he struggled, he realized that today was a lot like last night. The thing that soaring is better than was – well, at the moment, neither one was very satisfying and both had become a lot of work. *Maybe I should just stay in the garage and make toys for the grandchildren,* he thought.

One solution to getting up and staying up in gliders, as we all know, is to spend the big bucks and buy a self-launcher. The problem is that our health insurance doesn't cover it, even though the mental health benefits are obvious, and even though it might keep us away from Deadly Junk Food for a few hours.

He thought, *Maybe I should talk to my doctor and see if it's right for me.* But so far he hadn't because he'd heard that the FAA didn't like these drugs, and worried a bit about this. Did they do something bad?

Risk v. Risk

The relative risks of these parallel pleasures are somewhat different. Soaring results in death, we hate to admit, at a higher rate per hour than coal mining. Death from genitive congress is rare, and seldom violent (but rarely accidental). You pretty much can't catch any diseases while thermalling, or get in a family way, partly because most gliders are essentially narcissistic, having only one chair, for The Most Important Person. I hope, given the lack of autopilots in gliders, that no one has joined the mile-high club in a two-seat ship.

We were asked, in a recent email, to discuss the use of masculine self-launching medication in soaring. This did not at first seem particularly interesting, as it's not very likely that any pilot will get confused on which stick operates the elevator; and there's good reason not to disturb the one that's useless for flying, for when that little multipurpose hose firms up, the urethral sphincter closes and prevents bladder relief. It's hard enough to let it go while reclining under a cloud without taking drugs that make it harder.

FAA restrictions.

On the other hand, the FAA prohibits the use of the 3 tumescence tablets in pilots: 6 hours after taking sildenafil (Viagra™), 36 hours after vardenafil (Levitra™ – this should be 6 hours), and 36 hours after tadalafil (Cialis™). There are reasons for this. These medications, like all drugs, have extra effects, "side effects," which may be adverse to adroit piloting.

I asked my Regional Flight Surgeon what data these restrictions were based on, but the specialist who made the rules has gone on to other duties, and his replacement hasn't seen the files.

Possible bad experience.

Even so, we can use our noggins to figure out why caution is reasonable:

These things started life as *antihypertensives* – blood pressure medications, and they *do* reduce the blood pressure. People have been known to get lightheaded with standing, or faint, or die from this. At a minimum, G-tolerance is reduced, and even though you might feel fine toddling around the gliderport, the 2 Gs of a 60-degree bank might not be such a good idea.

Second, the nose is lined with erectile tissue. Normally, we breathe mainly through one nostril, and these alternate subtly, rhythmically at long intervals. These drugs can very naturally create a stuffy nose. A stuffy nose is associated with middle-ear congestion, which can cause severe ear pain or vertigo with the large changes in altitude that we seek on a good soaring day.

Third, as they dilate arteries a bit, they may cause a throbbing headache. If severe, this can distract a pilot from useful details, such as whether the gear is down, or which direction is home.

Fourth, sildenafil and vardenafil affect the rods and cones, and may change color vision, with bluish discoloration and difficulty with blue/green color discrimination. This is more annoying than harmful, but the FAA prefers we have normal color discrimination while flying.

Fifth, these drugs are gotten rid of by the liver using an enzyme, cytochrome P450, that processes many drugs. The cue can get crowded if you take other medications that use this enzyme: There are many, such as cholesterol-reducing statins, blood pressure medications, hormones, and most psych meds (these are never used by soaring pilots, are they?). The result is that the effect of all such medications is then increased, and their duration of action (including side effects) lengthened. Grapefruit juice famously inhibits this enzyme, raising related drug levels, possibly to toxicity.

Many other medications directly inhibit the work of cP450, and many others stimulate its production. If you want to check this out, don't ask your doctor or druggist, go to http://en.wikipedia.org/wiki/CYP3A4 and read the list. Make a

list of the generic names of all the drugs you take and look for them in the lists.

End of preamble

You can stop reading here if all you want is the answer to the question. Now, I'll embark on the usual "this is how it works" portion of this column.

What are Meds?

Medications are chemicals that have a desired effect. Our bodies themselves are a complex soup of organic and inorganic chemicals, arranged in a very complicated and dynamic, self-maintaining structure.

Medications are promoted as if they have only one effect, a chemical arrow shot through a biological bulls eye. The miracle of medicine is that each drug has only a few effects, not hundreds. In fact, much of the progress that's occurred in pharmacology during the past half-century has been to discover ways of making drugs more selective in their effects.

How drugs work.

In general, drugs act by altering the biochemical activity of cells. This occurs at one of three sites:

First, at the cell wall. Each cell has thousands of protein molecules embedded in its cell wall. These proteins may act as switches to regulate chemical processes inside the cell, or may trigger release of preformed chemicals to the fluids around the cell. Drugs that can attach to these proteins may either stimulate or block their activity.

Second, within the cell cytoplasm. Some drugs transition the cell wall, and interact with proteins or ions within the cell.

Third, in the nucleus. A few drugs enter the cell nucleus and affect the transcription of genetic material. This is a slow process; nuclear induction of new cellular enzymes takes about three months to be fully effective.

Drugs that are most specific in their actions are those which interact with only a particular protein, whether this is on the cell wall, in the cytoplasm within the cell, or in the nucleus. The specificity is related to the shape and electrical charge distribution of both the drug and its target molecule. Generally, this relationship has been discovered long after the drug is known to do something good. A few drugs have been designed for a particular molecular effect.

What on earth is Phosphodiesterase?

Glad you asked! If you truly want to know the details, look it up in wikipedia.org, and search images.google.com and open the web pages belonging to the most interesting illustrations. They are all complicated. Phosphodiesterases are found in every cell of the body. If you don't need the technical detail, here's an oversimplified precis:

The most common mechanism by which cells perform actions is that a specifically configured protein arrives at the cell (via the blood and intracellular fluid or delivered by a motile cell or a stimulatory cell such as a neuron), and there attaches to and thereby activates a complementary, specifically-configured protein in the cell wall. This "receptor" protein undergoes reconfiguration when its complement arrives. This triggers, typically, a sequence of tightly-regulated reactions within the cell.

For example, when insulin arrives at the cell wall, it binds to the head of an insulin-receptor protein; when this happens, the tail of the insulin receptor, within the cell, curls very precisely to begin a set of protein interactions – more than three dozen – with several effects, one of which results in another protein, the glucose transporter, being released from intracellular storage and straddling the cell membrane, where it sits, sucking in glucose. There are about a dozen proteins in the chain from the insulin receptor to the glucose transporter – giving us about a dozen ways to become insulin-resistant and acquire "adult-type" diabetes.

Many of these reaction chains are modulated by one of two proteins: cyclic adenosine monophosphate, (cyclic AMP or cAMP) or cyclic guanosine monophosphate (cyclic GMP or cGMP). When both are present in a cell, they typically have complementary effects, one amplifying an action (typically cAMP) and the other inhibiting (typically cGMP). The proteins in each cell that create actions are comparable to a complex dimmable light switch, in that the mechanism of the switch is irrelevant to the specific light or the means by which it's turned on; and this mechanism within the cell does not determine the action the cell is designed to perform.

Thus, cAMP and cGMP are merely common mechanisms for many different bodily functions.

These proteins are important in creating (or inhibiting) the response of each cell to the "signal" represented by the specific protein binding to its receptor on the cell wall. The influence of these proteins is in part regulated by degrading them. The protein that breaks them down is a phosphodiesterase.

The action of cAMP or cGMP can be prolonged by any drug that inhibits its breakdown: a phosphodiesterase inhibitor. Caffeine was one of the first to be discovered and is the best-known and most-used PDE inhibitor throughout the world. Caffeine is pretty non-specific, and basically jazzes up anything in which cAMP is involved, meaning that it has many effects. Wakefulness, increased blood pressure, rapid heartbeat, shaky muscles, and more.

There are 11 types of phosphodiesterases in various tissues in the body. Some act more to degrade cGMP, others cAMP, some both. PDE-5, the one most interesting to aging males, breaks down cGMP.

There are actually four forms of PDE-5 located in various tissues, such as brain, heart, lungs, colon, pancreas, and genitals. You know that these tissues have different functions. A PDE-5 inhibitor will affect them all, to some extent, depending on how selective it is. Six target tissues, six effects. The effect you want at the moment is the "therapeutic effect," the ones you don't are the "side effects."

For most uses of PDE-5 inhibitors, the genital changes are "effect" and the other changes are "side effects," but for some people reducing the blood pressure in the lungs is the important effect, or enhancing the relaxation of heart muscle.

In fact, these drugs were first developed to treat high blood pressure, and they do drop the blood pressure – a "side effect" if you didn't want it to

happen (fainting is so inconvenient, especially on those rare occasions when death follows).

Each of the 3 drugs used to enhance masculine tumescence has different selectivity, and chemists have discovered and synthesized many different phosphodiesterase inhibitor drugs (PDE inhibitors) of various types. Their effects depend on which phosphodiesterases are blocked and how strongly.

Effect vs side effect.

Most medications have a number of effects. The one we want to use is its "effect", the others are "side effects." One of my favorite old medications, doxepin, causes drowsiness, relieves pain, decreases stomach acid production, blocks the allergy protein histamine, slows urinary flow, dries up saliva production, slows bowel function, and eases anxiety. Which of these are today's "side effects" depends on what's today's problem. For example, doxepin may help a woman with a leaky bladder stay dry overnight (effect) but prevent the man with a big prostate from passing water at all (side effect).

When we can nail two different problems with one drug, that's a big bonus.

There are three PDE inhibitors sold that improve tumescence. They all inhibit PDE-5, which has several roles. They also inhibit other PDEs. This means that "side effects" can become "therapeutic effects."

For example, both sildenafil (Viagra) and vardenafil (Levitra) are potent PDE6 inhibitors (which are located in rods and cones), to cause the blue haze. Tadalafil (Cialis) inhibits PDE11, which is important in sperm production and motility, but not PDE6, so it doesn't produce color-vision changes but could affect fertility. PDE5 inhibitors are being used to treat pulmonary hypertension, high-altitude mountain sickness, memory dysfunctions, and cardiovascular diseases. PDE5 inhibition with sildenafil may be useful to treat heart failure, as it improves cardiac relaxation, the heart's recovery after injury, and thereby improves symptoms in patients.

Social consequences.

How often do we hear our pal say, "Soaring is better than sex," and then watch him assemble his single-seat glider. Maybe that explains something.

If we take a minute to think about our sport, we have folks at two extremes. One is the (often low-time) pilot who spends enormous amounts of time running around the gliderport taking care of details, towing, instructing, organizing meetings and banquets, serving as field safety office on the best soaring day of the year, and in general filling gaps.

These, my friends, are the people who keep the sport going. It's fun being with people, and rewarding. The personal tension is that all this support does reduce flight time.

At the other end of the sport is that occasional narcissist who drives in about an hour before trigger temp develops, assembles with as much help as can be coerced to lift a wingtip but forgets their names, groans if there's a wait for tow, and vanishes back into his micro-cosmos after stuffing the ship back in the

box. These folks always have a single-seater, preferably a self-launcher.

Discussion is useful.

When the little blue pills first came out, men started to ask for them, shyly at first. Each time, I'd ask, "How does she feel about this?" There was usually jaw-dropping, stunned, silence. I'd say, "It might be interesting to ask." Again, a pin could drop. Then I'd say, "You might want to try seduction." Blank look.

The prescription would be written, and after a year or two or five, Mr. Clueless would be back about something. I'd say, "Need a renewal?" He'd usually say something like, "No, I don't think there's interest on the other side of the bed."

Life works the same, no matter what the activity. We are designed to be social creatures – to be alone is painful: neurological research has shown that loneliness is as noxious as severe physical pain. Yet there's a natural tension because we are naturally self-centered. There is a secondary presumptuousness that other people, if they are aware, probably share our values, conclusions, enthusiasms, and goals. This would be wrong.

The most satisfying pleasure is intimacy with another person with whom we feel safe – who seems to like us as we are, in whose life we are interested and they in us, and with whom we can share ideas, communicate without struggle, and work as a team. It is in our nature to extend intimacy from one life area to another.

Men who are able to achieve intellectual and emotionally intimacy with a partner are far less likely to need the pharmacological tow than those who are alone even in a crowd. I have no cure for this, and no medication for it.

The only treatment I know of is to set aside what captivates me, and ask what's captivating the other person.

References

These technical articles are available on the Internet and provide nice summaries if you are interested:

Boswell-Smith V, Spina D, Page CP. *Phosphodiesterase inhibitors.* British Journal of Pharmacology (2006) v147,S252-257.

Ghosh R, et al. *Phosphodiesterase inhibitors: their role and implications.* International Journal of PharTech Research (2009) v1(4), 1148-1160. ISSN: 0974-4304

Keravis T & Lugnier C, *Cyclic nucleotide phosphodiesterase (PDE) isoezymes as targets of the intracellular signalling network: benefits of PDE inhibitors in various diseases and perspectives for future therapeutic developments.* British Journal of Pharmacology (2012) v165, 1288-1305. DOI:10.1111/j.1476-5381.2011.01 729.x

Acknowledgements

Thanks to the pilot who'll I'll keep anonymous for asking the question, and to Lewis Shaw for the quotation from Lao Tzu. Thanks to Dr. David Schall, FAA Great Lakes Regional Flight Surgeon for looking into the FAA database on these drugs. Thanks to Paul Randall for finding some important typos.