

HOW I DISCOVERED VIAGRA — BUT LOST THE NOBEL PRIZE

Michael Nevins

An obituary that appeared this week in the New York Times (September 7, 2023) reminded me of an incident that I experienced early in my medical career, some fifty years ago. The news item announced the death at age 86 of pharmacologist Ferid Murad who in 1998 shared the Nobel Prize with two others for their research into the cardiovascular effects of nitric oxide. According to the obituary, Dr. Murad made his discovery in part by accident. So had I.

My partner and I, both recently having completed cardiology fellowships at Mount Sinai Hospital, were striving to build a two-man practice in northern New Jersey while, at the same time, feeding our rapidly growing families. In order to supplement our paltry incomes, we shared a part-time job as research assistants in a hypertension clinic at the Bronx Veterans Administration Hospital. The purpose of our work was to study the effects of various new drugs on veterans who suffered from severe high blood pressure.

Between experimental protocols we were free to manage these men with whatever drugs were readily available. One day I read an article in a cardiology journal which suggested that when confronted with a patient who is refractory to even a large dose of then the most powerful anti-hypertensive agent Ismelin (guanethidine), blood pressure control could be enhanced by adding Dibenzyline (phenoxybenzamin), one pill a day. This is an alpha-adrenergic blocking drug that, among other effects, dilates blood vessels and, according to what I read, could augment the hypotensive effect of Ismelin.

I had such a patient; I'll call him Patient "X". He was a heavy-set, rather surly vet whose BP usually hovered around 240/140, regardless of what new treatment we tried. This was an astounding number and yet he seemed to be totally unaffected by any medical complications. He'd reliably take whatever we prescribed, returned on schedule and offered no comment. Because we were between research projects, he was taking a maximum dose of Ismelin — BP 240/140 and no complaints. I reasoned, why not add a little Dibenzyline and see what happens? He grumbled something, but agreed to take the combination and return in a week for follow-up.

Right on schedule, X returned the next week but he appeared different. He seemed uncharacteristically talkative, even cheerful. He told me that he really liked the new medicine and wanted more. Wow! I couldn't wait to measure his blood pressure, surely it would be dramatically lower. Not so. 240/140. I rechecked. The same. I asked X how come he liked taking the new drug so much? ***"Doc, It gave me back my nature."***

I was stunned. Only then I remembered that one of the major side effects of Ismelin is impotence — what nowadays is called erectile dysfunction. I'd never thought to ask and he'd been suffering in silence, but now he felt like a new man. So did I. I excitedly began composing in my mind a report to the *New England Journal of Medicine* about my serendipitous finding. But true scientist that I am, I decided that at least I should try the drug on a second patient to see if the effect was reproducible. Alas, the next patient reported no life-altering reaction, nor was his BP lowered.

About two decades after my experiment at the Bronx VA, Sildenafil, the active ingredient in Viagra, was developed by Pfizer as a possible dilator of coronary arteries for patients with angina pectoris. But during clinical trials, an unexpected side effect detected by an observant nurse was that many of the men were laying on their stomachs, embarrassed to reveal that they were developing erections — the wrong blood vessels were dilating! By 1998 Viagra was approved by the FDA for erectile dysfunction and within 20 years more than 62 million men worldwide were using the “little blue pill.”

I won't attempt to explain the complicated pharmacokinetics, but it appears that alpha-blockers and nitric acid share dilating effects on certain blood vessels, indeed the two chemicals may interact. These days, nitric acid can be bought over the counter for treatment of ED — Amazon will ship it (Nugenix) directly to your home “in discrete packaging.”

But I still wonder what ever happened to Patient X — I may have given him back his nature, but what about his life? 240/140!

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