Sir, “Despite the constant negative press covfefe”
- Donald Trump.

While the world continues to debate the “true meaning” of covfefe,[1] there is at least one professional group which understands what usage of this noun conveys. Endocrinologists encounter a lot of covfefe in their daily work. As they strive to improve the hormonal and metabolic health of the people they care for, they are faced with unexpected opposition.

The qualified endocrinologist is well-trained to identify and manage hormonal dysfunction. What he or she may not be prepared to handle, however, is the vast amount of misinformation that individuals and the community harbor. Such misinformation, or “hormonal hearsay,” may range from harmless to life-threatening. It is this hormonal hearsay[2] that we describe as “endocrine covfefe.”

We approach the phenomenon of endocrine covfefe through a medical student’s prism. The etiology of endocrine covfefe is multifactorial. Self-styled endocrinologists, practitioners of complementary and alternative medicine (CAM), fitness gurus, manufacturers of non-proven “medicinal” products, and misguided laypersons; all churn out their own version of endocrine fables and myths. The pathogenesis of endocrine covfefe is similar to that of an infectious disease. Spread by word of mouth (i.e., by the ear) in the past, covfefe is now created on the internet. Social messaging media, such as Twitter, WhatsApp, and Messenger, have played an important role in bringing down the incubation period of covfefe to virtually zero.

The natural course of covfefe is marked by heterogeneity and multidirectional spread. Covfefe, akin to a syndrome, includes a constellation of untruths, half-told truths, and misconstrued truths, which masquerade as scientific facts. Covfefsters utilize this uncertainty to market unproven “hormonal” therapy for longevity, vitality, youthfulness, and sexuality. Such activities add spice to the otherwise drab, and somewhat boring, world of medical covfefe.

Clinical features of covfefe are diverse in their presentation. In general, endocrine covfefe has a faster rate of spread as compared to other medical covfefe. This is especially true if discussion revolves around diseases which are common (diabetes), which impact social wellbeing (obesity), or personal wellbeing (sexual dysfunction). Conditions which require self-discipline for treatment are exceptionally prone to covfefian slander: Popular hearsay usually revolves around interventions which do not require exercise or calorie restriction to manage illness. A favorite target of endocrine covfefe science is injectable therapy, such as insulin and growth hormone. In the hands of these covfefe science, life saving drugs are given demonic or asuravian properties which project them (and their prescribers) as destroyers, rather than protectors, of human health.[3]

Endocrine covfefe has a definite anti-salutogenic effect on the health of the community. This may range from mere discomfort or wastage of resources (e.g., eating live fish, procuring camel milk to cure diabetes)[4] to life-threatening situations (e.g., shifting from insulin to CAM in type 1 diabetes; sudden stoppage of steroids).

The management of endocrine covfefe is a matter of debate. No fool proof management strategy has been developed so far. Leading endocrine and diabetes organizations have well-developed patient/public education websites,[5,6] to spread public awareness, and minimize e-hearsay, but tangible results are yet to be seen.

While the rest of the world figures out what covfefe means, endocrinologists must campaign to contain, or ban, endocrine covfefe. In concordance, our fellow medical professionals must work to minimize medical covfefe in particular and health covfefe in general.

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Sir,

Loss of pancreatic \(\beta\) cells is a pathological hallmark of both type 1 and type 2 diabetes mellitus; however, no specific therapy targeting this defect is yet available. A paradigm shift with such a molecule has always been awaited. Verapamil – a nondihydropyridine calcium channel blocker used in the treatment of hypertension, angina, and tachyarrhythmias, particularly atrial fibrillation – has been observed to show some hope in preventing \(\beta\) cell loss in diabetics by inhibiting thioredoxin-interacting protein (TXNIP).

TXNIP was first cloned in 1994 and the relation with \(\beta\) cells was elucidated in 2002. Pancreatic \(\beta\) cells have a poor antioxidant system and are highly susceptible to oxidative stress. TXNIP inhibits thioredoxin – a redox protein/antioxidant system [Figure 1], and thereby induces oxidative stress. \(\beta\) cells TXNIP expression is strongly induced by glucose and is increased in diabetes. The overexpression of TXNIP in \(\beta\) cells has been shown to promote \(\beta\) cell apoptosis and reduce insulin production, [2] as shown in Figure 1.

Genetic deletion or pharmacological inhibition of TXNIP seems to be protective against diabetes. In animal studies, the calcium channel blocker verapamil has been shown to prevent \(\beta\) cell apoptosis in streptozocin-induced diabetic mice; it supposedly promotes \(\beta\) cell survival and improves glucose homeostasis by inhibiting TXNIP expression. [2,3]

Recently, verapamil has also been shown to decrease fasting plasma glucose in diabetic patients in an observational study of 4978 patients – REasons for Geographic And Racial Differences in Stroke (REGARDS). Type 1 diabetics, and type 2 diabetics on insulin with or without oral drugs, who also received verapamil had fasting serum glucose levels that were 24 mg/dL lower than those who did not receive verapamil (\(P=0.039\)), [4] correlating with approximately 1% reduction in glycated hemoglobin. In another study of patients with no prior diabetes, oral verapamil use was associated with a lower incidence of type 2 diabetes (6.41 vs. 8.07 per 1000 per year) compared with other calcium channel blockers. [5]

Following REGARDS observation, a randomized controlled trial (NCT02372253) is ongoing to study the effect of verapamil in \(\beta\) cell survival in type 1 diabetics focusing on functional \(\beta\) cell mass, exogenous insulin requirements, glycemic control, and TXNIP expression in peripheral blood monocytes. [6]

The future of clinical studies holds prospect for verapamil as well as other TXNIP inhibitors to come up as \(\beta\) cell saviors in preventing and treating diabetes. If it proves...