An internist and clinical pharmacologist, Dr. Duggal is a clinical associate professor at the University of Washington and Medical Director of the Liberty Bay Internal Medicine center. He is an international authority on drug therapy and clinical pharmacology and has presented over 1000 lectures to healthcare professionals on various medical and pharmacy topics, including therapeutics, drug interactions, diabetes, pain control, hypertension, hormone replacement therapy, and lipiddology. Dr. Duggal is also a consultant/researcher for the Pharmacist Letter, Prescriber’s Letter, and Natural Medicine Comprehensive Database. Holding numerous certifications, Dr. Duggal is a certified diabetic educator, psychiatric pharmacist, geriatric pharmacist, hypertension specialist, and lipid specialist. He is a fellow of the Royal College of Physicians of Canada and fellow of the American Society of Consulting Pharmacists.

UTASIP: Hypogonadism has generally been considered a largely underdiagnosed condition. With the steadily growing elderly population, do you feel that there have been improvements made in detection and diagnosis of this somewhat age-related condition? Or, have the baby boomers highlighted the problem of underdiagnosis even more?

Dr. Duggal: Hypogonadism, or the relative decrease in testosterone, has become a very hot and debatable topic in medicine today. The average life expectancy of the American male is now approximately 76 years, and this older population is expected to grow. The concept of “a baby-boomer wave” is actually a gross understatement. For the healthcare force of America, the increasing population of older Americans is no small wave, but a tsunami. And, this educated and well-financed population of male men is not just happy to grow older. They want therapy so that they can be well in their later years. This paramount need for better quality of life is largely responsible for the significant press that the underdiagnosed condition of hypogonadism has received. And, certainly, there have been improvements made in detection techniques. Tests for free testosterone, total testosterone, and sex hormone binding globulin are now easier to order than they were a few years ago, but they are still underutilized by clinicians. And, what still remains unclear is the optimal testosterone level for each individual man. That’s where a thorough clinical evaluation can shed some light. I think it’s necessary to ask about symptoms and investigate certain clinical parameters, in addition to ordering laboratory tests. I certainly would suspect hypogonadism and measure testosterone levels in patients who present with what I call the “grumpy old man syndrome.” Basically, we have to start asking our patients more questions in order get a more accurate clinical picture. And, with the advent of the Internet and consumerism, our patients are certain to come knocking on our doors looking for answers. Thus, I feel it is best for clinicians to have a more extensive clinical approach to functional hypogonadism and its therapeutic management.

UTASIP: What can healthcare professionals, specifically pharmacists, do to raise awareness of hypogonadism among patients and perhaps even among unsuspecting primary care physicians?

Dr. Duggal: Keeping abreast of the ever-changing
face of clinical medicine and pharmacy is a challenge for even the best clinicians. I consider us pharmacists to be in the front lines of healthcare and, in order to provide useful resources to our patients, it is imperative that we know the signs and symptoms of hypogonadism, such as fatigue, mood swings, decreased libido, and changes in hair pattern and muscle mass. Developing information pamphlets, public seminars, and educational sessions, in addition to enlisting local physician champions to help educate the masses, are all excellent ways to introduce this relatively new and emerging area of medicine and pharmacy to the public and our peers. Furthermore, it is crucial for pharmacists to be well versed in the different modes of delivery of the various testosterone products, thus they can teach patients how to use the medications correctly. Finally, pharmacists are a great resource to turn to when investigating medications. They can easily review patients’ medication profiles and identify common medications (ie, opioid analgesics, digoxin, and spironolactone) that may be causing secondary, drug-induced hypogonadism. This is an excellent form of a medication management service that pharmacists can provide to clinicians and patients. This issue of University of Tennessee Advanced Studies in Pharmacy includes some of the common drugs that may cause a secondary drug-induced hypogonadal state. Screening for these drugs is a vital aspect of the workup for hypogonadism, and yet, it may easily be overlooked by primary care physicians—but not by an astute pharmacist.

UTASiP: Considerable controversy exists over the concept of a male climacteric or “andropause.” Growing evidence indicates that some aging men have reduced production of testosterone accompanied by associated symptoms. Some studies indicate that the problem may be related more to coexisting conditions. What are your thoughts on this matter?

Dr Duggal: The concept of andropause, which has been referred to in the literature by numerous names, including “grumpy old man syndrome,” partial androgen deficiency syndrome, and late-onset hypogonadism, is certainly controversial but it is also a very real symptom complex for aging males. The diagnosis is made by recognizing the existence of a constellation of symptoms, identifying certain signs in an aging patient, and finally doing confirmatory laboratory tests to rule out secondary causes of the symptom complex and ruling in hypogonadism. It should be noted that this symptom complex is extremely common and underdiagnosed. In fact, some estimates indicate that less than 5% of men with features of hypogonadism are ever identified or treated by their clinician. Although some men will have classical symptoms and confirmatory test results, these relatively straightforward cases are not the norm in medicine. More often, functional hypogonadism is a multifactorial phenomenon of relative decreased testosterone levels that hover in the mid to low range in a patient who also has some secondary risk factors, such as the metabolic syndrome, diabetes, obesity, cardiovascular disease, smoking, or chronic opioid use. This is a more realistic clinical scenario. And, the big question is whether I can treat the reduced testosterone and, at the same time, affect changes in these other associated conditions.

UTASiP: Can you comment on the growing relationship between testosterone deficiency and the metabolic syndrome?

Dr Duggal: The relationship between metabolic syndrome and hypogonadism is a fascinating one. As you are aware, metabolic syndrome is a constellation of features first coined in 1988 and formally recognized by the National Cholesterol Education Program in 2001. This devastating state is characterized by high triglycerides, low high-density lipoprotein cholesterol, central obesity, hypertension, and impaired fasting glucose. The condition is highly correlated with insulin-resistant states. I have coined metabolic syndrome the “heart attack–diabetic want-to-be.” It is estimated by the National Health and Nutrition Examination Survey database that approximately 24% of the US population has metabolic syndrome and
approximately 44% of patients older than the age of 60 years suffer from it. It has been recently recognized that many male patients with metabolic syndrome also have low testosterone levels. The physiological mechanism for this phenomenon is not entirely clear, but there are some theories. In one explanation, the increase in fat cells causes an aromatase estrogen-like reaction that, in effect, counteracts the effects of testosterone. Another hypothesis builds on the concept of physiological stress and subsequent endocrine changes. In a series of events over the long term, the increased stress status in the body leads to slightly increased levels of corticosteroids (cortisone) in the blood. This abundance of steroids eventually leads to an accumulation of fat in the abdomen. The association between metabolic syndrome and testosterone deficiency appears to be strong. If we identify male patients with features of the metabolic syndrome, we should also evaluate them for symptoms of testosterone deficiency and strongly consider doing their hypogonadism. Monitoring the medications is also important and should be done regularly. As we learn more about the dynamic relationship between testosterone and the aging male, we will have to refine our monitoring parameters. Finally, payment from third-party payers is also an issue for some patients.

UTAS/P: There is concern that testosterone supplementation may raise the risk of benign prostatic hyperplasia (BPH), and even prostate cancer. Do you feel the risk is substantiated? And, on a related topic, how would you approach a patient who has hypogonadism as a result of various treatments used to cure his prostate cancer?

Dr Duggal: This is probably the single most controversial area in testosterone replacement therapy in the aging male. If you are an evidence-based clinician, you should be aware that there is not a single study that has shown that administering exogenous testosterone accelerates development of prostate cancer or BPH. However, from a theoretical perspective, it is possible that stimulating the prostate gland with testosterone may increase the risk of prostate cancer or BPH. The logic behind this hypothesis is sound and, because prostate cancer appears to be a very slow-growing cancer, we may not see a change in the short- and long-term studies. It's important to assess each patient for potential prostate cancer, and if you find it, obviously testosterone replacement therapy would be contraindicated. The presence of BPH is considered a relative risk, thus one can still use testosterone therapy but monitor symptoms of urinary obstruction and prostate-specific antigen (PSA) levels. However, I must reiterate that based on the breadth and veracity of the available data, testosterone replacement has not been associated with the acceleration of prostate cancer.

Utilizing testosterone replacement in a patient who has been “cured” of prostate cancer is really more of a medical-legal question whose answer ultimately lies with each individual patient. First, you must define “cure,” then you must evaluate the relative impact of hypogonadal symptoms on a patient's quality of life, and finally, you need to clearly outline all the risks and benefits of testosterone treatment and alternative
options to a patient, thus he can make an informed, well thought-out decision. Because most guidelines would contraindicate the use of testosterone in patients with prostate cancer, anytime, we are in a real therapeutic dilemma. I think testosterone therapy may be considered in a patient cured of prostate cancer if that patient’s life may be substantially improved by it and if the patient assumes the risk (however small it may be) after the physician explains the potential consequence in detail. Ultimately, the patient has to decide for himself.

UTASiP: There are various preparations of testosterone available, including intramuscular injections, oral agents, scrotal patches, and transdermal patches and gels. How do you go about choosing which preparation to use on which patient?

Dr Duggal: I avoid using oral preparations because they have significant first-pass effects in the liver, and as a result, they are associated with liver enzyme elevation and hepatic adverse effects. These preparations have largely fallen out of favor among most clinicians. Intramuscular injections assure adequate delivery but are painful at times, produce wide swings in testosterone levels between injections, and have variable effects. The options that I am left to turn to are scrotal patches, transdermal patches and gels, and buccal delivery systems. All of these products are topical, have minimum first-pass and liver effects, cause some product transference with skin contact, exhibit minimum fluctuations in blood levels, and cause only minor skin irritation. For these reasons, topical testosterone products have really become the treatment modality of choice for most clinicians. Cost and personal responses to therapy are the factors that I consider when choosing one topical product over another. I also take into consideration patient support and education that a product manufacturer may offer, provided the company has evidence to support their product claims.

UTASiP: Some patients who present with erectile dysfunction are being identified as having underlying hypogonadism. Does erectile dysfunction often accompany hypogonadism and how are these patients being managed in terms of combining testosterone replacement therapy and phosphodiesterase (PDE)-5 inhibitors?

Dr Duggal: I find that most patients with erectile dysfunction are placed on PDE-5 inhibitors and are not worked up for a possible hypogonadal state. This certainly is a significant clinical omission. First and foremost, you want to provide the correct therapy for the correct diagnosis. If a patient with hypogonadism is just given a PDE-5 inhibitor for his erectile dysfunction, then, essentially, he is not being treated for his underlying etiology. One might suspect possible hypogonadism in patients who do not benefit from PDE-5 inhibitors, and at that point, it would be wise to do a more thorough clinical workup. In patients with hypogonadism and erectile dysfunction, the combination of a PDE-5 inhibitor and testosterone therapy may provide more complete and satisfactory results. In addition, data show that you may be able to reduce the dose of a PDE-5 inhibitor if it’s used concurrently with testosterone.