Sports Pharmacy

DECODING THE SCIENCE OF ELITE HUMAN PERFORMANCE

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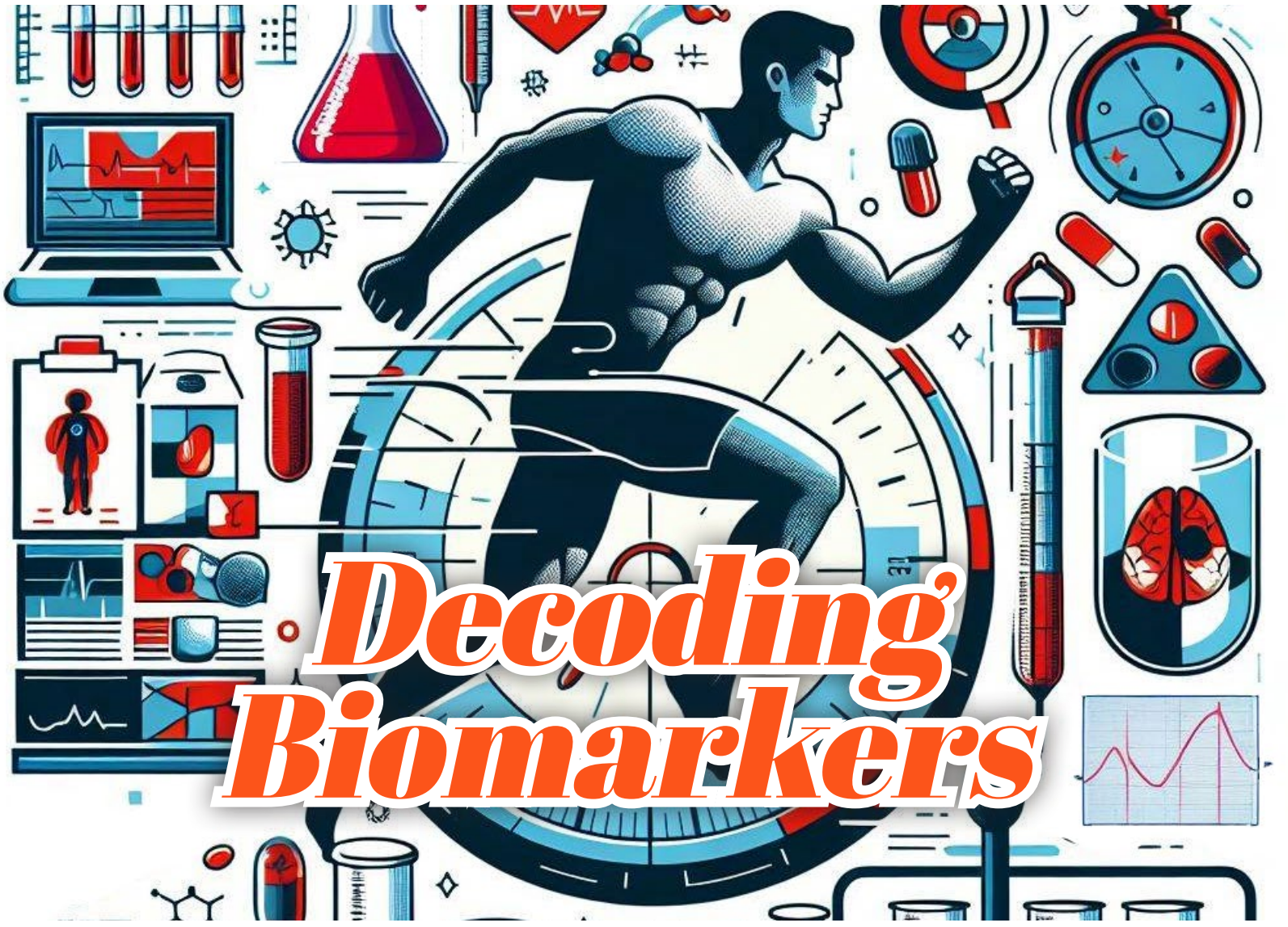

Decoding Biomarkers

Unlocking the Potential: Hormone Testing for Optimizing Athletic Performance

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Letter From the President

Dear Sports Pharmacy Magazine Subscribers,

The start of 2024 has been an exciting time for our organization. We first want to extend our gratitude for your unwavering support as a subscriber to our magazine. Just recently, we had the pleasure of launching our new sports pharmacy enterprise, the Sports Rx Network to better serve our members. We have been able to deliver immense value to our student and allied health members who have already signed up to join the network.

Our focus and goal is to continue to foster meaningful relationships with athletes and health care professionals to deliver robust clinical value to better support athlete health, safety and performance. Our team has taken the time to work very diligently in creating clinical resources and educational vehicles to deliver this information in an efficient and accessible manner.

The future of sports pharmacy is blazing and will continue to rapidly evolve. Advancements stemming from health wearables, to blood biomarker testing for health and peak performance, to genetic testing for personalized medicine and nutrition. I believe the list will continue to expand with advanced technology. We invite you to continue to explore our platform for updated sports pharmacy news and information.

Once again, thank you for being an essential part of our community. Your continued support propels us forward, and we are genuinely excited about the future of Sports Pharmacy Magazine. Cheers to innovation, and a shared passion for the fascinating intersection of sports and pharmacy.

Warm regards,

Brandon Welch, PharmD, CPh, CWC
President, Sports Pharmacy Network
Clinical Sports Pharmacist

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SPORTS RX NETWORK
DISPENSING THE SCIENCE OF ELITE HUMAN PERFORMANCE

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Are CGMs the Next Sweet Spot in Athletics?

By Kelsey Rasmussen, PharmD

AUTHORS BIO:

Kelsey Rasmussen, PharmD, BCGP, is a clinical pharmacist at Peninsula Community Health Services, an FQHC in Washington state. In this role, she performs disease state management in anticoagulation, diabetes, and hypertension. She provides comprehensive pharmacy services, optimizing patients' medications in the ambulatory setting. She serves as a wellness ambassador and is adjunct faculty at the University of Washington School of Pharmacy and Washington State University School of Pharmacy. She is a member of WSPA, ASHP, U.S. Sports Pharmacy Group, and the USA Deaf Soccer Association and serves as a board member on the ASCP Washington and Safer Fields for All. She played soccer at the University of Washington (NCAA D1), where she completed her undergraduate degree in economics and earned her Doctor of Pharmacy degree. She is passionate about sports pharmacy and holds sports nutrition, wellness, and Drugs in Sport certificates. She enjoys building rapport with patients and athletes, empowering them to be proactive and optimizing their wellness, health, and performance. Kelsey enjoys living on the Peninsula, which provides the opportunity to cycle, paddleboard, ski, and play on the water with her family.

Continuous glucose monitoring (CGM) devices are currently approved by the FDA in the United States (US) for use by the 38 million people living with diabetes.1 Glucose monitoring has come a long way since the 1960s, evolving from the first in-office blood glucose test to the advancement of CGMs that provide 24/7 data on a minute-by-minute basis.2 Competitive athletes and biohackers who strive for optimal health and performance are likely familiar with CGM devices and may be wearing one now. Wearable fitness technology offers health metrics for monitoring health, performance, and preventative care. This article will evaluate the effectiveness and accuracy of CGM devices in athletes and non-diabetic individuals while highlighting the pharmacists' role in data assessment.

Effectiveness and Accuracy of CGMs for Athletes and Non-Diabetic Individuals

Blood glucose monitoring continues to advance, with increasing accuracy in measurement. In 2016, CGMs were FDA-approved to make treatment decisions, marking a shift from fingerstick self-monitoring blood glucose (SMBG) testing.[3] Several factors must be considered when assessing the accuracy and reliability of CGM devices compared to traditional blood glucose meters (BGMs).

CGM devices currently require a prescription in the US. Athletes and non-diabetics can consult their healthcare providers or enroll in telehealth wellness subscription services, which can furnish the necessary prescription and CGM device. Additional health services like nutrition services and health coaching may be added benefits of telehealth wellness subscription services.

CGMs are not approved for use in sports or healthy adults in the US. Abbott, manufacturers of FreeStyle Libre, partnered with Supersapiens, a sports performance technology company, and in 2020 created the world's first CGM biosensor designed explicitly for athletes aged 16 and above. However, it is unavailable in the US.[4] The Libre Sense Glucose Sport Biosensor is similar to the FreeStyle Libre3 Sensor, providing continuous glucose reading every minute, streaming glucose data with a dynamic range of 55-200 mg/dL.[4] The FreeStyle Libre3 Sensor and other sensors are incompatible with the Supersapiens program.

Whether obtained as a prescription from your pharmacy or through a wellness subscription service, the CGM device, Dexcom or FreeStyle Libre, adheres to the same standards approved for patients with diabetes. Dexcom and FreeStyle Libre systems are the most common on the market in the US. CGMs are factory calibrated; thus, they do not require user calibration. The disposable sensors are worn for 10 - 14 days on the back of the upper arm (Dexcom G7, FreeStyle Libre), abdomen (Dexcom G6), or upper buttocks (Dexcom G6 & G7, ages 2 to 17 years old).

Any CGM and BGM approved has an acceptable range of accuracy. CGMs use the mean absolute relative difference (MARD) to measure accuracy, and BGM accuracy is assessed according to the FDA

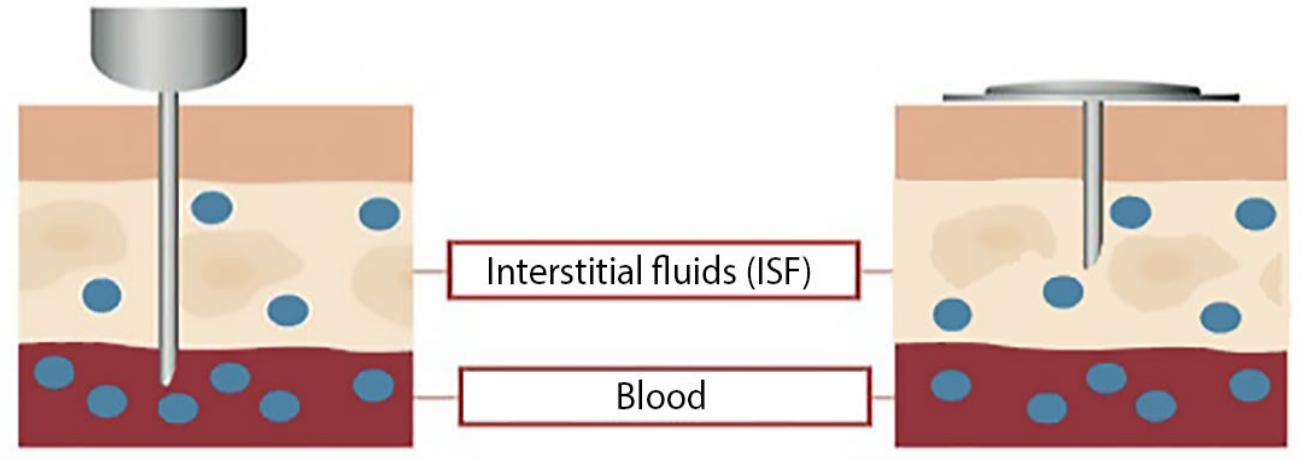
Sensor interference may also occur due to medications and supplements.

and The International Organization for Standardization ISO 15197:20136.[5,6] These standards are not directly comparable. The MARD measures the average difference between a device measurement (or test result) and the reference measurement at normal to high glucose levels. This means that the lower the MARD, the better, and most CGMs have a MARD of less than 10%.[7] Integrated CGMs (iCGM) include FreeStyle Libre2, FreeStyle Libre3, Dexcom G6, and Dexcom G7, which are set to a higher standard by the FDA to be integrated with other devices, such as an automated insulin delivery system.[7,8] Most BGMs that are FDA-approved are within 15% of the true lab value 95% of the time.[9] If the blood glucose sample is 100 mg/dL, then BG is accurate if it is 85 or 115 mg/dL, and if the CGM sample is 100 mg/dL, then iCGM is accurate if it is 80 or 120 mg/dL.[10] Dexcom informs users of the "20 Rule," aka (20%/20 rule), to ensure their CGM device is accurate.[11]

Another difference is the physiological lag time between blood glucose (BG) and interstitial glucose (IG).[12] The sensor is placed under the skin, measuring the glucose in the interstitial fluid (IF) compared to BGMs, which measure capillary blood glucose. Under steady state conditions, there is little difference between IG and BG.[13,14] The lag time is most evident during rapid periods of change, such as after eating or during or after exercise. The sensor glucose (SG) will always lag BG but is close enough that insulin can be adjusted off SG results. During episodes of hyperglycemia, BG will be higher than SG, and during hypoglycemia, BG will be lower than SG. This lag may vary by 5-25 minutes, depending on physiological changes during exercise, muscle contraction, changes in vascular flow, hydration, body temperature, and body acidity.[12,13,15,16]

Another situation to be aware of is false lows, mainly occurring at night if the sensor is compressed by sleeping on the side. When this happens, the IF decreases due to the pressure applied, and the sensor's needle detects less fluid and, therefore, less glucose.[11,17] The IF glucose should return to a closer match once pressure is relieved.

Sensor interference may also occur due to medications and supplements. Known substances that interfere with CGMs differ by brand, including acetaminophen (Tylenol), ascorbic acid (Vitamin C), and hydroxyurea, which may become co-oxidized at the sensor and potentially cause falsely elevated glucose levels.[12,13]



Comparison of BG sample from fingerpick and SG sample from CGM sensor. SG reflects the glucose in the interstitial fluid surrounding the cells compared to the BG sample from capillary blood.

Source:https://www.freestyle.abbott/kw-en/discover-freestyle-libre/why-freestyle-libre-/difference-between-sensor-glucose-and-blood-glucose.html

Overall, CGMs provide reliable real-time insights, capturing a more comprehensive picture of glucose variability than A1C and SMBG. Similar to diabetes management therapy, changes are not based on one glucose value but on trends. The ADA includes recommendations for CGM metrics such as % Time in Range (TIR, the % of time spent 70-180 mg/dl) or the Glucose Management Indicator (GMI), which is an estimate of A1C that is derived from a 14-day CGM report for routine assessment of glucose levels.[18] CGMs help provide insights regarding glucose patterns and trends. Their effectiveness can be enhanced by integrating other devices that offer fitness metrics, such as heart rate monitors, smartwatches, rings, and sleep trackers. This integration enables athletes to correlate glucose levels with exercise intensity, quality of recovery, and sleep patterns to provide a more comprehensive landscape of their overall wellness and performance.

Benefits and Limitations of CGM for Athletes and Non-Diabetics Individuals

The utilization of CGMs is on the rise among individuals without diabetes, aiming to optimize their health through 24-hour data collection. Glucoregulatory hormones include insulin, glucagon, amylin, glucagon-like peptide-1 (GLP-1), glucose 1-phosphate, glucose-dependent insulinotropic peptide (GIP), epinephrine, cortisol, and growth hormone, which all play a crucial role in glucose homeostasis, maintaining glucose within target ranges. According to the ADA, a normal fasting blood glucose is under 100 mg/dL and postprandial less than 140mg/dL.[18] Various triggers, such as diet, exercise, stress, illness, alcohol, and poor sleep, impact the secretion of these hormones. CGMs provide immediate visual feedback on lifestyle choices, revealing the diverse effects of carbohydrates and lifestyle habits on glucose metabolism.

Athletes can use CGMs to experiment with different meals, activities, supplements, or recovery methods, gauging their impacts on blood sugar levels and identifying patterns to guide decisions. CGMs may be beneficial in endurance sports to ensure adequate carbohydrate intake to optimize glycogen stores and glucose availability, helping avoid fatigue or "hitting the wall." This often results from muscle glycogen depletion and reduced blood glucose concentrations. Athletes can experiment with various meals, activities, and training to track if they're on a glucose rollercoaster or sense hunger after a spike in BG. Stress, irrespective of food intake, induces a glucose response mediated by adrenergic and catecholamine hormones, which affect blood glucose and insulin function.[14] Integrating CGM data with daily logs empowers users to assess how mood, sleep, exercise, and nutrition influence glucose patterns over time.

CGM devices provide a wealth of glycemic data, empowering users to achieve glycemic stability. Blood glucose patterns provided by CGMs offer intuition that may aid in stress management, nutrition, performance, recovery, and disease prevention. Monitoring metabolic responses before, during, and after exercise enables the identification of trends in training and recovery strategies. Therefore, more extensive research is necessary to explore the full potential and benefits of CGMs in healthy, athletic, non-diabetic individuals.

Nocturnal hypoglycemic events can disturb sleep, and hypoglycemia may help measure energy levels. Real-time insights allow athletes to experiment with fueling strategies and how diet impacts blood glucose and energy levels. Depending on observed trends, it may validate or expose the need to adjust meal timing, macronutrient ratios, and portion sizes to ensure adequate energy supply for optimal performance.

CGMs can also assist in preventative care. Sometimes there are no apparent symptoms of prediabetes. Out of the 38 million people living with diabetes in the US, 1 in 5 don't know they have it.[1] Fluctuations in blood glucose can serve as a screening tool for insulin resistance, prediabetes, chronic inflammation, oxidative stress, and liver or kidney problems.[16,19,20] This heightened awareness empowers individuals to proactively implement lifestyle changes or seek further education and discussions with healthcare provider(s) to mitigate future health risks.

Most randomized controlled data from CGMs are from Type 1 diabetic patients, with positive results in reducing A1C levels and episodes of hypoglycemia.[8] A limited number of studies have been conducted on healthy adults, and their small sample sizes constrain the scope of findings. Therefore, more extensive research is necessary to explore the potential benefits of CGMs in healthy, athletic, non-diabetic individuals.

Sensor limitations encompass potential local skin irritation from the adhesive, limited range of connectivity to a smartphone or reader, sensor placement, risk of detachment in the water or high contact sports, and loosening due to sweat. Most sensors are water resistant, and the Dexcom G7 sensor is waterproof. Both should perform the same in salt or freshwater. Altitude effects stemming from extreme temperature and humidity may impact sensor accuracy. Abbot and Dexcom sensors are safe to wear while traveling by plane. During preflight screening, the sensors are safe to be placed in carry-on or luggage but not tested in all airport scanners, and

alternative screening should be requested when going through security.[21,22]

The Role of Pharmacists in Data Assessment

CGMs offer abundant data, but their effectiveness hinges on comprehending, integrating, and applying the information practically. Sports pharmacists can play a vital role in this process by assessing glycemic metrics and analyzing CGM and corresponding wearable data. Athletes can collaborate with clinical sports pharmacists who can provide valuable insight, develop action plans, offer education on areas of concern, and create a comprehensive clinical perspective to optimize health and performance.[8] Additionally, sports pharmacists can contribute to putting more pieces of the puzzle together for the patient-athletes by identifying potential factors impacting BG levels (e.g. medications, underlying causes of low or high BG, stress, lifestyle factors, and physical activity).

Most CGM devices use the glucose oxidase approach, and sports pharmacists can review medications and supplements to help identify interfering substances. Pharmacists may also assist in selecting the most suitable CGM devices, depending on their sport. Through an interdisciplinary approach, sports pharmacists collaborate with the athletes and their care team to create a comprehensive plan, and provide guidance and practical application of the data collected from CGMs.

Conclusion

CGM devices furnish athletes with real-time updates, enabling dynamic adjustments to help sustain a competitive edge, extend their careers, and facilitate informed health decisions for optimal energy. SG lags the BG due to the interstitial measurement of glucose, which is particularly noticeable and is most evident during transitions like times of change, including post-meals and exercise, and does not diminish the practicality and value of the information provided by the CGM.

Imagine how a run or bike ride with elevation offers a new perspective and landscape. CGMs offer 24/7 glucose monitoring, providing athletes and non-diabetic individuals with precise and practical insights, revealing a comprehensive holistic view of glucose patterns. This broader perspective can uncover opportunities for improving diet, sleep, recovery, and disease prevention. Collaborating with an athlete's care team, a clinical sports pharmacist can facilitate the creation of action plans that integrate CGM data to achieve health and performance optimization.

CGM Device	Sensor Wear Duration (Days)	Data Transmission	Sensor Data Memory	Bluetooth Range	Water Performance	Interfering Substance
Dexcom G6[23, 28]	10	Every 5 minutes	3 hours	20 feet	Water resistant (up to 8 feet up to 24 hours)	Acetaminophen (Tylenol), > 4 grams/day + Hydroxyurea +
Dexcom G7[24, 28]	10	Every 5 minutes	24 hours	20 feet	Waterproof (up to 8 feet up to 24 hours)	Acetaminophen (Tylenol), > 4 grams/day + Hydroxyurea +
Freestyle Libre 2[25,28]	14	Every minute (scan at least once every 8 hours to transmit data to app)*	8 hours (stored every 15 minutes)	20 feet	Water resistant (up to 3 feet up to 30 minutes)	Ascorbic Acid (Vitamin C), > 500 mg/day +
Freestyle Libre 3[26,28]	14	Every minute	14 days (stored every 5 minutes)	33 feet	Water resistant (up to 3 feet up to 30 minutes)	Ascorbic Acid (Vitamin C), > 500 mg/day +

*FreeStyle LibreLink app to version 2.10 not yet available in the United States[27]
+Falsely elevated CGM reading compared to BG

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Biomarkers for Athletic Performance – What are They?

By Dr. Brandon Welch, Pharm.D., M.S.(c)

AUTHOR BIO:

Dr. Brandon K. Welch is an experienced licensed wellness pharmacist that holds his doctorate in pharmacy from the University of South Florida and his bachelor degree in biomedical sciences with a focus in biochemistry. He is the wellness pharmacist for Baptist Health where he works collaboratively with the Miami Dolphin's and Florida Panther's team physician to help enhance athletic performance and reduce risk of illness. His passion in connecting metabolic health with human performance led him to pursue his Master's degree in physiology and kinesiology with a concentration in human performance and athletic development. His expertise lies in functional training, metabolic health, sports nutrition, sports medicine, and sleep therapy. He utilizes science based medicine and literature to help maximize his clients training performance and daily lifestyle. He's worked with several clients, helping them lose weight, improve performance, improve their sleep cycle, muscle building, and appropriate nutrient supplementing.

Biomarkers are biological molecules that can provide us with objective information about what is happening inside our bodies. Biomarkers can include things like metabolites, proteins, electrolytes, hormones, and other small molecules. Measuring and tracking these substances can give critical insights into our bodily functions, including our physical state, risk of disease, or progression of diseases or conditions. Biomarkers may also be a great way to assess athletic performance.

Can Biomarkers be Used to Track Athletic Performance?

A newer use case for biomarkers involves athletic performance. Some services that provide genetic and biochemical testing to understand athletic performance and recovery during training are already available. However, there are several challenges associated with using biomarkers in this context.[1] Some of these difficulties include:

- The inability of a single biomarker to characterize broad physiological functions. For example, something as broad as "recovery" cannot be traced with a straightforward molecule
- The lack of reference ranges for specific types or groups of athletes
- Variability between individuals regarding biomarker measurements. Every person is different, and thus, there is no "one size fits all" for biomarker benchmarks

Because of the intricacies associated with biomarker testing in athletic performance, researchers need to take a more holistic and dynamic approach to testing and identifying biomarkers.

Several factors influence athletic performance, including metabolic health, endurance, inflammation, hydration, nutrition, injury status, and muscle status. Based on thorough research, experts have identified key biomarkers for each factor that can help characterize and understand athletic performance.

Nutrition and Metabolic Health Biomarkers

It is no secret that nutrition plays a significant role in our ability to perform physically. Likewise, it is essential to have biomarkers indicative of nutritional and metabolic status to understand how to best fuel our bodies for peak performance. We can divide up potential nutritional biomarkers into those that are considered macronutrients and micronutrients.

Macronutrients

Macronutrients can help us contextualize sports performance include glucose, fats, and proteins.[1] Let's review:

- *Glucose.* Our bodies utilize glucose, also known as sugar, for energy. Our glucose levels fluctuate depending on what and when we eat, if we are working out, and the amount of energy we have. For example, consuming carbohydrates increases our glucose levels, increasing energy and improving performance during physical activity. Low blood sugar levels can negatively impact performance. Thus, glucose may be a critical nutritional indicator for athletes
- *Fats.* Sugar is not our only source of energy. Fat is a medium in which our

> Vitamin D is essential for bone health, protein synthesis, and muscle function.

body can store and relinquish energy, specifically during extended periods of physical activity. Certain fats like omega-3 fatty acids can minimize muscle soreness and inflammation during recovery while supporting nerve and muscle connections during training. Thus, omega-3 fatty acids can be a marker for recovery and training

- *Protein.* We all know how important protein is for building and growing muscle. A lack of protein can lead to decreased muscle mass and, thus, impaired performance. Certain indicators in our blood, such as albumin, can help quantify an athlete's protein intake

Glucose, fats, and proteins are essential to training and recovery. Monitoring these biomarkers can inform us of an athlete's nutritional status and, thus, predict performance.

Micronutrients

Micronutrients are vitamins and minerals that our body needs; however, they are in smaller amounts than macronutrients. Although we do not need a ton of micronutrients, we can still experience deficiencies that impact physical performance. Important micronutrient biomarkers can include[1]:

- *Vitamin D.* Vitamin D is essential for bone health, protein synthesis, and muscle function. Athletes typically strive for levels greater than 50 ng/mL of vitamin D, as these levels can increase aerobic performance and, thus, general athletic ability
- *B complex vitamins.* B vitamins include niacin, thiamin, pyridoxine, biotin, folate, choline, and pantothenic acid. B vitamins contribute to energy metabolism, supporting the breakdown and synthesis of carbohydrates, proteins, and fats. Likewise, they are vital to converting food into energy for peak performance
- *Vitamin E and beta-carotene.* Vitamin E is an antioxidant, meaning that it protects against cellular damage. Beta-carotene converts to vitamin A, another antioxidant that minimizes muscle injury and supports muscle recovery
- *Magnesium.* Magnesium contributes to nerve function, muscle function, and energy metabolism. Deficiencies can cause muscle problems, including weakness and spasms.
- *Iron.* Iron is essential for transporting oxygen throughout the body. When deficient, athletes may experience anemia, fatigue, cognitive impairment, and immune deficiencies
- *Zinc.* Zinc is critical for wound healing, protein synthesis, immunity, and cell functioning, making it particularly important for endurance athletes

Hydration Biomarkers

Adequate hydration is critical to maintaining water balance within the body. Water is involved in numerous biochemical reactions contributing to cell volume regulation, body temperature, body weight, and more.

We typically refer to our sense of thirst when considering how much water we should intake. However, research indicates that thirst usually occurs when we are already dehydrated. Thus, hydration biomarkers can help prevent dehydration and increase performance during exercise.[1]

Blood Biomarkers

In the context of blood biomarkers for hydration, two essential parameters are osmolality and sodium levels. Blood osmolality, for example, is one of the best ways to understand hydration levels, as it is susceptible to changes in hydration status. Additionally, because dehydration affects the kidneys, another great indicator is urea nitrogen to creatinine ratio.

These markers can be useful to determine if someone is dehydrated before exercise. They can also be assessed after exercise to understand how much fluid someone needs to recover properly.[1]

Urine Biomarkers

A few markers of dehydration in the urine include arginine vasopressin (AVP) hormone, urine-specific gravity (USG), and urine osmolality (UOsm). However, a more straightforward way to assess hydration is by simply checking the color of your urine. A lighter color indicates adequate hydration, whereas a darker color may indicate dehydration.[1]

Image source: Review—Point-of-Care Urinalysis with Emerging Sensing and Imaging Technologies - Scientific Figure on ResearchGate. Available from: https://www.researchgate.net/figure/Example-of-a-urine-color-chart-for-hydration-assessment-141_fig9_338348460 [accessed 13 Feb, 2024]

Muscle status biomarkers

The quality of our muscle tissue, including its composition, size, structure, and metabolic capacity, contributes to our ability to perform physically. Your strength, power, endurance, and fatigue reflect your muscle's ability to recover from exercise-induced damage. There are several biomarkers available related to muscle function. Experts recommend to consistently evaluate these biomarkers , as there is typically inter-person variability in these parameters.[1]

Endocrine markers

The following hormones are important to understanding athletic performance[1]:

- *Testosterone.* Testosterone is necessary for red blood cell production, protein synthesis, and replenishing glycogen
- *Cortisol:* This works against testosterone, preventing protein synthesis when elevated.
- *Dehydroepiandrosterone (DHEA):* In female athletes, DHEA changes are associated with over-training
- *Sex hormone-binding globulin (SHBG):* SHBG increases as a result of exercise.
- *Growth hormone (GH):* GH activates anabolism through the synthesis of muscle proteins and preventing protein breakdown

Amino acids

As previously mentioned, protein is essential for exercise. Amino acids, the building blocks of protein, can indicate if one's muscles are getting enough nutrients. For example, the amino acid taurine is necessary for muscle growth. Taurine deficiencies can hinder proper muscle development and function. Other amino acids like leucine, valine, isoleucine, tryptophan, and glutamine can also signal muscle status.[1]

Other markers

Intense physical activity causes muscle damage, the muscles release an enzyme known as creatine kinase (CK) as a result.[1] CK, as well as other substances like urea nitrogen and myoglobin, can indicate protein breakdown and consequent muscle damage.

Cardiovascular biomarkers

Iron is an important biomarker for cardiovascular health, contributing to oxygen transport and aerobic metabolism[1]. Both processes are essential to maintaining cardiovascular endurance during exercise. Thus, monitoring iron levels and related markers like transferrin saturation, ferritin, and iron binding capacity can signal cardiovascular status while training.

Inflammation biomarkers

Inflammation is an important marker of athletic performance and, thus, is something many athletes want to track. To understand inflammation, we should look at cytokines and growth factors. Elevations in pro-inflammatory cytokines such as IL-6, IL-10, IL-1b, IL-8, TNF-a, and IL-12p40 can indicate inflammation[1]. There are no established ranges or thresholds for these cytokines; thus, athletes should establish an individual baseline and fluctuations to understand these changes better.

Injury biomarkers

Although assessing athletic performance is important, equally is monitoring our susceptibility for injury. Biomarkers in this space are not as clear, however, some do exist. For example, IGF-1 is associated with fracture risk and low bone quality. In females, low concentrations of IGF-1 correlated with increased risk of fracture. Bone mineral density (BMD) may also play a role.

Some studies have shown elevations in inflammatory markers like IL-6, IL-8, and CRP after anterior cruciate ligament (ACL) injuries. Biomarkers of brain injury may include S-100B and neuron-specific enolase, as these are elevated after head trauma.[1]

Conclusion

In summary, biomarkers are an efficient way for our bodies to signal normal or abnormal function. They can be instrumental for monitoring athletic performance, specifically when considering biomarkers related to nutrition, hydration, cardiovascular health, inflammation, injury, and muscle status.

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Micronutrient Testing - What Sports Pharmacists Need to Know

AUTHOR BIO:

Sean Casey RD CSCS is a registered dietitian, movement coach and member of the Evolve Wellness Science Team at Hometown Pharmacy of Wisconsin. He specializes in sports nutrition, nutraceuticals, and proactive care.

By Sean Casey, RD, CSCS

The pursuit of optimal athletic performance often extends beyond conventional assessments. Here, micronutrients play a pivotal role in unlocking athletes' full potential.

You may ask critical questions such as "Are my patient-athletes consuming enough magnesium to meet the demands of their training regimens?" or "Is the Omega-3 consumption of an individual athlete enough for peak health?"

If you ponder these questions and more, you are not alone. Answering these questions is where micronutrient testing comes into play. This article delves into key studies and actionable insights to enhance your practice and patient-athlete well-being.

Study #1:

Iron Status and Physical Performance in Athletes (2023)

Iron serves many critical roles within the body, most importantly carrying oxygen as part of the hemoglobin proteins found in red blood cells.

"What does the current research show concerning iron status and athletic performance?"

This is a question Solberg and Reikvam asked in their 2023 literature review.[1] More specifically, they sought to find out:

1. What blood markers reflecting iron status should be monitored by those looking to maximize athletic performance?
2. Do "optimal" levels differ for athletes vs. the general population?

Although many factors reflect iron status in the body, Solberg and Reikvam note ferritin, a protein that stores iron, as the primary marker of importance in their review. Iron deficiency comes in two different forms, with and without anemia.

1. Iron deficiency without anemia (NIDA) is when ferritin levels are low (< 30 mg/L) but circulating hemoglobin levels are still normal (>130/120 g/L in men/women)
2. Iron deficiency with anemia (IDA) is when both ferritin levels and hemoglobin are low (<30 mg/L and < 130/120 g/L in men/women, respectively)

In NIDA, oxygen-carrying capacity is still normal. Despite normal blood oxygen levels, the patient-athlete may experience symptoms such as reduced concentration, impaired physical performance, and fatigue due to iron's role at the cellular level.

Research on what the optimal levels is for athletes is still mixed. Yet, to optimize health, wellness, and performance; levels may need to be at least 40-90 ng/mL, with some research indicating even higher levels.

What would be signs that a patient-athlete needs a ferritin test? As a sports medicine professional, I first look for unexplained fatigue, especially if diet, sleep, and training load are appropriately managed.

In addition to drops in athletic performance, mood disorders may also be a sign of iron deficiency.[2] Along with supporting oxygen delivery to the brain, iron plays a vital role in synthesizing var-

The journey toward personalized nutrition in sports medicine is exciting, with immense potential for refining athlete well-being.

ious neurotransmitter pathways (serotonin, dopamine, noradrenaline) and influences neurogenesis, including the production of brain-derived neurotrophic factor (BDNF).As sports medicine professionals, how can we improve iron status in clients/patients?

Encourage the consumption of 8 mg for men and 18 mg for women of iron daily. In pregnancy, the daily iron recommendation increases to 27 mg daily.[3] If supplementation is required, ferrous bis-glycinate is more bioavailable than traditional ferrous sulfate.[4]

Heme iron is the most bioavailable form of iron obtained from eating meat. Iron in the non-heme form can also be obtained by eating plants (whole grains, chickpeas, spinach).[3] Various dietary factors affect the absorption of dietary iron. For instance, foods containing high amounts of vitamin C, such as citrus, enhance iron uptake, whereas polyphenols present in tea and coffee can inhibit absorption.

Low energy availability (LEA) can independently decrease iron absorption by impacting circulating levels of hepcidin, a protein that blocks iron absorption within the gut. A crossover study by Hennigar et al. found that seven days of LEA (45% of estimated daily caloric needs) increased hepcidin levels while decreasing iron absorption in 10 healthy male subjects (mean age – 22 years old) following intense physical training vs. completing the same physical activity following seven days of energy balance.[5]

Sports pharmacists should also recommend routine checking of vitamin D levels to optimize the oxygen-carrying capacity of the blood and iron status. Vitamin D supplementation helped preserve hematological variables in elite male traditional rowers.[6] This is accomplished through supporting the body's ability to undergo erythropoiesis.

Study #2:

Associations Among Omega-3 Fatty Acid Status, Anxiety, and Mental Toughness in Female Collegiate Athletes (2017)

Navigating anxiety can be challenging, especially for student-athletes juggling the pressures of daily life, the weight of exams, and the expectations of performing in front of a crowd.

Preliminary research shows that Omega-3 fatty acids impact cognitive function and mood in the general population. Wilson and Madrigal performed a cross-sectional study to see if Omega-3 levels similarly correlated with anxiety and mental toughness in female collegiate athletes.[7]

In a study, 54 female Division 1 NCAA off-season athletes representing basketball, soccer, rifle, and golf participated. Omega-3 levels were assessed via the Omega-3 Index (O3I), and anxiety was measured using the Beck Anxiety Inventory (BAI), looking at general anxiety levels, as well as the Sport Anxiety Scale (SAS)-2 and Mental Toughness Scale (MTS).

Upon study conclusion, the median O3I score of participants was 4.9% with an interquartile range of 4.2-5.4%.[7] To help put these numbers in perspective, optimal O3I scores are considered in the ~8-12% range. Here, cardiovascular events, mortality, cognitive function and many other risk factors are reduced. An analysis by Harris et al., which reviewed 10 cohort studies, estimated that improving O3I from 4% to 8% would reduce the risk of fatal cardiovascular events by 30%.[8]

Regarding anxiety, Wilson and Madrigal found O3I scores negatively correlated with BAI ($r = -0.32$; $p = 0.02$), reflecting improved mood with higher Omega 3 levels.[7] Findings also supported that blood levels of docosapentaenoic acid (DPA), a specific type of Omega 3 fatty acid, positively correlate with mental toughness

(r=0.27; p = 0.049). No correlation was found between O3I and sport-specific anxiety.

While higher O3I has many benefits, a big one for athletes is supporting better mood in athletic settings.

Study #3 and #4:

Pitfalls in the Interpretation of Blood Tests Used to Assess and Monitor Micronutrient Nutrition Status (2022) and Challenges in the Diagnosis of Magnesium Status (2018)

Within the last 5-10 years, greater emphasis has been placed on complete micronutrient blood analysis to optimize patient-athlete outcomes and performance. These tests often go beyond the well-established vitamin D, iron, and O3I nutrient testing, extending into most vitamins and minerals within our body.

As sports medicine professionals, it's essential to ask ourselves the question,

"Are these micronutrient tests measuring what we think they're measuring, and if so, what are optimal levels for human performance and disease prevention?"

Berger, Talwar, and Shenkin noted the challenges with blood micronutrients in a 2022 literature review.[9] Standard serum micronutrient levels reflect acute intake, and inflammation levels can influence results. Additionally, serum plasma levels for most nutrients are preserved within a narrow window. To this end, they recommend measuring Red Blood Cell (RBC) levels for micronutrients as these results may better reflect long-term micronutrient intake vs. fluctuating based on acute factors. Measuring blood micronutrient levels via RBCs may better reflect long-term nutrient intake vs. plasma levels. The accuracy of RBC is still often called into question.

Workinger et al. noted in a 2018 literature review that assessing magnesium levels via RBC levels was preferential to serum levels. More long-term studies (~ 3 months) are needed to establish this measurement technique. Additionally, magnesium RBC studies often failed to validate their methods by correlating their values with inter-compartmental samples from urine or muscle. Claims that magnesium RBC testing accurately reflects total body stores are premature. Further research publications are needed to differentiate optimal, inadequate, or deficient values related to magnesium RBC values.

Uncertainty surrounding many blood micronutrient tests, such as magnesium and other nutrients, underscores the importance of employing clinical judgment alongside examining other blood markers, clinical symptoms, and information from the patient-athlete.

For instance, if a patient-athlete's serum and RBC magnesium levels look normal but present with restless legs, anxiousness, and migraines, sports medicine professionals should still consider increasing dietary magnesium through food and nutritional supplements. Reevaluating after a given period is vital to assess if the intervention positively impacted symptomology.

Wrapping Things Up

Micronutrient testing holds great promise in personalizing nutritional and supplement plans for patient-athletes. However, sports medicine professionals must be aware that outside of iron, vitamin D, and Omega-3 nutrient testing, much research needs to be carried out to clearly define both the validity and "optimal" levels for patient athletes.

Anticipate a future filled with numerous outstanding research that will further enhance our understanding of blood micronutrient testing and its application in optimizing athletic performance. The journey toward personalized nutrition in sports medicine is exciting, with immense potential for refining athlete well-being.

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Unlocking the Potential:

Hormone Testing for Optimizing Athletic Performance

By Dr. Jessica Beal-Stahl, PharmD

AUTHOR BIO:

Dr. Jessica Beal-Stahl, PharmD, is the founder of The Athlete's Pharmacist company, tying her passions of athletics and pharmacy together where she works privately with clients to improve their performance in sport and life. She received her Doctorate of Pharmacy from Mercer University in 2009 and has been practicing as a Director of Clinical Services at Hobbs Pharmacy in Merritt Island, Florida, since graduation. Jessica also knows what it's like to be a high-level athlete, having played D1 volleyball, medaled internationally in Olympic weightlifting, and set at 41 years old a world record in Olympic Weighting for snatch in her age/weight class. She holds additional certifications in Integrative Medicine, Nutrigenomics, and Sports Nutrition.

Have you ever wondered how hormones affect athletic performance? There is no arguing that hormones play a crucial role in athletic performance and overall well-being. Diving into the intricate interplay between hormones and athletic performance won't give you superpowers, but it can yield valuable knowledge in harnessing their powers. By tracking and learning to decipher the subtle indicators of hormone fluctuations, athletes and healthcare providers can gain critical knowledge to improve performance, train efficiently, improve recovery, and spot early signs of overtraining.

The process of testing hormone levels is scientifically complex and nuanced, and the question of whether to test or not and which testing method is superior to another is debated by healthcare providers and scientists alike.

For athletes, hormones are essential for regulating energy levels, muscle growth, recovery, immune function, menstrual cycles, metabolism, mental health, and overall well-being. Hormones such as growth hormones and thyroid play a key role in supporting a healthy body composition and bone health, while testosterone is essential for building muscle mass and strength. Additionally, releasing certain hormones during exercise can promote favorable adaptive changes, improving performance.

Laboratory medicine in sports is an important preventative and protective science, fundamental for evaluating an athlete's condition. However, most sports research is still under lock and key (partly because gold medals depend on it often), and very little has been done focusing on women. Among 12,511,386 participants in 5,261 manuscripts published in six sport and exercise science journals between 2014 and 2020, females accounted for 34% of the study population; only 6% of total publications were conducted exclusively on females.[1] One reason is the impact of constantly changing hormone levels in females.

Hormone testing can provide insight into how an individual's unique hormonal profile may impact their ability to reach specific performance goals, allowing for more informed and targeted training approaches. Testing can help athletes and healthcare providers identify any underlying hormonal imbalances that could affect their performance and track changes over the season.

The interplay between workload and recovery is important for athletes to prevent injury while maintaining the highest level of competitiveness and growth. This balance can be monitored and optimized using laboratory medicine and other data (i.e., wearables, athlete symptoms, and performance), particularly in identifying overtraining. It has been

> *Hormone testing can provide insight into how an individual's unique hormonal profile may impact their ability to reach specific performance goals, allowing for more informed and targeted training approaches.*

established that healthy athletes have adaptations to their hormonal conditions.[2] By addressing identified imbalances through targeted treatment plans, athletes can experience improved energy levels, increased muscle mass, and enhanced recovery, leading to better overall performance.

Several key hormones are important for athletic performance.[3] These include:

- *Testosterone* – essential for building muscle, increasing strength, maintaining energy stores and oxygen capacity, and decreasing fatigue
- *Growth hormone* – important for muscle growth and repair
- *Cortisol* – regulates the body's stress response, impacts muscle breakdown, affects metabolism, blood sugar, and water/salt balance
- *Thyroid hormone* - regulated metabolism, cardiac function, calcium homeostasis, and energy levels
- *Insulin* – impacts blood sugar levels and affects muscle growth and repair
- *Estrogen and Progesterone* – play a crucial role in bone health injury prevention, impact thyroid health, inflammation, mental health, and menstrual cycle

Hormones and Performance

Overtraining syndrome (OTS) is when there is a imbalance between training and recovery. If training continues before an athlete recovers, fatigue accumulation occurs. In the early stages of OTS, athletes report fatigue and decreased performance, which can be overcome with a longer recovery period. If OTS continues, long-term problems brew and changes to the body's physiology take place, taking months to correct.[4] Sex and adrenal hormones must be used as biomarkers of OTS in athletes. They can be used if an athlete is in the early or late stages of OTS.[5] Estradiol and testosterone levels and their ratio have also been shown to be diagnostic in OTS.[6] Increasing sex-hormone binding globulin (SHBG) in response to lowered testosterone levels from under-recovery can be indicative of OTS.[7] In female athletes, OTS can also show low levels of estrogen and progesterone, manifesting as menstrual disorders.[4]

Suppose athletes have a mismatch between the energy going in (nutrition) and energy going out (movement). In that case, athletes can find themselves in the spectrum of Relative Energy Deficiency in Sport, known as RED-S. Previously, this was known only as the Female Athlete Triad. One of the pillars of RED-S is hormonal changes, as the body chooses survival over reproduction. Female athletes often see menstrual changes or amenorrhea as an outward sign, but negative hormone changes in labs often show up sooner.

Hormone Variation During Menstrual Cycles

Men and women vary in many ways regarding sports and exercise. Still, the biggest difference, which can have far-reaching effects, is the cyclical change in hormones that occur in women throughout the menstrual cycle. Almost half of all women believe their menstrual cycle hurts their training and performance.[8]

We are beginning to learn about the impacts of the menstrual cycle on female athletes. While it's never a bad day for a PR or gold medal performance, athletes can't help if competitions are on particular days of the menstrual cycle. Knowing the ebbs and flows of our cycle can help keep motivation up. Also, ensure athletes have menstrual cycles, as up to 40% of female athletes falsely believe that losing their period is a normal or positive sign of being an athlete.[9]

Tracking hormones for female athletes can help note changes over time or if symptoms arise. It can also help with screening for menstrual irregularities, polycystic ovary syndrome, heavy menstrual cycles, and fertility issues.

Different Types of Hormone Testing

Hormone testing allows a better understanding of how the body operates under the surface and unravels the complicated internal reality that symptoms alone can't always reliably reveal. Four commonly used tests for hormone levels are blood serum, dried blood spot, saliva, and urine. Each has advantages and disadvantages, and there is likely no single "best" method for evaluating hormone levels.

Saliva

Saliva tests present a straightforward and accessible method for hormone assessment, particularly because they are easy to collect. Patient athletes can also easily provide multiple samples by simply spitting into a tube over a day, making it a practical and user-friendly option. International researchers initially employed saliva tests in remote areas where blood samples were impractical due to stability. In 1990, they were redefined for home test kits and direct-to-consumer testing.

Saliva testing helps measure the hormones available to use in tissue vs blood serum, which identifies levels of hormones circulating in the bloodstream. Research shows that saliva hormone levels often do not reflect serum blood levels for many female hormones.[10] Saliva tests are not the preferred method for assessing hormones in young women with menstrual irregularities, as they often have naturally lower levels of hormones in their saliva. Saliva is not helpful with testing hormones administered sublingually or transmucosal, as it can concentrate in the salivary glands and give falsely elevated results.

Blood serum

Serum blood tests are the oldest form of hormone testing and probably the most conventional method. Established reference ranges for both female and male hormones help interpret results. Insurance companies often cover this type of test.

> *Testing hormone levels is not just a tool for optimizing performance, but a window into the broader landscape of health and well-being.*

In serum testing, a blood sample is taken via a laboratory blood draw and sent to a lab for analysis. Once In the lab, they determine the concentration of specific hormones in the bloodstream. Most serum tests measure the level of "free" hormone, which is the hormone that can easily enter the cell; "total" hormone, which is attached to substances that carry hormones in the bloodstream; or a calculated combination of both free and total levels of hormones.

This method's limitation is that it does not accurately reflect bioavailable hormones, the hormones that are active in the organs and tissues. The collection method can also make these tests difficult, logistically challenging, and time-consuming depending on what hormones are being tested, for example, cortisol over the day or hormones throughout a menstrual cycle.

Blood Spot

Initially developed in 1960 to screen newborns for phenylketonuria (PKU) with a heel stick, the dried blood spot (DBS) test is simple and convenient for testing hormones. DBS test kits require you to prick your finger, drop it directly onto a filter card, and let it dry. The card is then mailed in for analysis, making it suitable for home testing. Once at the lab, samples are rehydrated and tested similarly to blood serum.

Dried blood-spot testing measures hormone levels in your small blood vessels (capillaries) vs whole blood, which evaluates venous blood levels. It's a small — but important — distinction, as there are likely variances in hormone levels throughout the circulatory system.

One distinct advantage of DBS over whole blood (serum) is that DBS is stored as dried blood and rehydrated for analysis; blood serum is analyzed in its original form. Conversely, DBS has a longer shelf life but is more limited in the variety of hormones and other analytes it can test accurately for.

Urine

Urine testing is hormone testing that allows practitioners to assess how the body metabolizes hormones. This provides an opportunity to identify risks when hormones are not breaking down optimally in the body.

Urine collection can occur in two ways, but all involve collecting multiple samples of urine multiple times a day in the privacy of your home. Most commonly, with hormone testing, urine is collected on a small piece of filter paper, dried, and mailed to the lab for evaluation.

Urine samples are not a direct measure of bioavailable hormones but measure hormones and their metabolites.[11] An analogy would be measuring how much food people eat by going through their trash cans. Hormone levels in urine can be affected by many variables, including kidney function, diet, and drug use (of any kind). The Endocrine Society, American Association for Clinical Chemistry, and the Partnership for Accurate Testing of Hormones have complained about the lack of standardization for accurately measuring hormone metabolites, especially those at deficient concentrations.[12,13] Research supports taking four dried-urine spots throughout the day is an effective alternative to 24-hour urine collection for measuring cortisol.[14]

Which is the best type?

In short, there is no "one size fits all" option when it comes to hormone testing, and many variables are involved in dealing with hormones including:

- Symptoms
- Medical history
- Current medication regimen
- Lifestyle
- Suspected hormone imbalances
- Personal preferences and limitations

Examining all these elements and considering how they work together is critical. But it takes more than simply reading lab levels to put pieces together; often, more in-depth study of hormones is needed. We are all unique as people and athletes. In some cases, using more than one type of hormone test could even be beneficial.

Conclusion

With a thorough understanding of an individual's hormonal profile, healthcare professionals can start working on dietary modifications, supplementations, training adjustments, and correcting imbalances to optimize performance and overall health. By addressing everyone's unique hormonal needs, our experts can help their patients and athletes achieve better health outcomes and reach their performance goals more effectively.

If you are an athlete and think you may be experiencing a decrease in performance, loss of muscle mass, or just not feeling yourself, it's a good idea to begin recording symptoms. Identifying hormone imbalances and designing an effective treatment plan can be complex and go beyond lab reports. Healthcare providers can work with sports pharmacists, trainers, and nutritionists to create a comprehensive plan for regaining balance and health.

I recommend labs in both off-season, and if problems arise or you feel like you are "hitting the wall" during the season, you have a baseline comparison to help understand what is happening. Some athletes will also test during the season to be aware of changes and adjust. Overall, getting a general health baseline of your hormonal and nutritional status is important annually.

But, of course, there's no magic pill when it comes to peak performance. It's a combination of training, nutrition, rest, and well-being. Hormones intricately weave into the fabric of athletic performance. Testing hormone levels is not just a tool for optimizing performance, but a window into the broader landscape of health and well-being.

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