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<p>In recent years, autologous biological preparations have emerged as a growing area of medical innovation in interventional orthopedical procedures and surgical interventions. These cellular therapies are often referred to as orthobiologics and are derived from patient's own tissues, such as blood, bone marrow, and adipose tissue to prepare platelet-rich plasma (PRP), bone marrow concentrate, and adipose tissue concentrate, respectively. In this article, we will emphasize and discuss the physiological variability of autologous PRP bioformulations regarding their effectivity in tissue repair. Furthermore, recent developments concerning platelet dosing, potentially effecting immunomodulation, and pain killing will be described.</p>	
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<p>In recent years, autologous biological preparations have emerged as a growing area of medical innovation in interventional orthopedical procedures and surgical interventions. These cellular therapies are often referred to as orthobiologics and are derived from patient's own tissues, like blood, bone marrow, and adipose tissue to prepare platelet-rich plasma (PRP), bone marrow concentrate (BMC), and adipose tissue concentrate (ATC), respectively. In this article, we emphasize and discuss the physiologic variability of autologous prepared BMC and ATC for the delivery of mesenchymal stem cells to support tissue repair processes.</p>	
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<p>Orthobiologic procedures are based on altering the microenvironment of musculoskeletal tissues to induce an anti-inflammatory effect and reduce pain, promote healing of these tissues, or provide mechanical support. Allograft tissues have these inherent qualities and can be used as such. This could provide patients whose own autologous tissues may be compromised or have contraindications to harvesting an alternative to treat their orthopedic conditions. Although these allograft therapies are promising, they lack high-quality clinical studies and regulatory guidelines currently limit their use.</p>	

Medical Concerns in Orthobiologics Procedures

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Peter C. Yeh and Prathap Jayaram

Orthobiologics have shown immense treatment potential in many medical fields including sports medicine, musculoskeletal disorders, and pain management. As with the case of any medical procedures and treatments, there are potential side effects or caveats that physicians and patients should be cognizant of. Nevertheless, the use of orthobiologics does not seem to have consistent severe side effects and do not have increased risks with transmissible disease, immune-modulated reactions, or oncologic processes.

Evidence-Based Approach to Orthobiologics for Osteoarthritis and Other Joint Disorders

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Katarzyna Herman and Alberto Gobbi

Osteoarthritis and cartilage lesions are a major cause of functional limitations which is why the goal of biological treatment is to preserve the native joint to delay the onset of OA. As a result of improvements in surgical techniques and technology, treatment options are more and more available, allowing the treatment of a whole range of injuries, from minor to extensive lesions both acute and chronic. In chondral lesion treatment, restoring hyaline-like cartilage provides improved durability of repaired tissue and desirable wear characteristics. Biological cell-based cartilage restoration treatment was developed to address the need for the long-term viability of repaired tissue. These procedures provide a reliable source of chondrocytes, whether directly or through the differentiation of multipotent precursor cells, capable of producing hyaline-like cartilage, with the minimal formation of fibrocartilage tissue. However, if arthritic changes begin biological therapies offer possibilities to delay. This chapter aims to discuss and give insights into these regenerative, joint preservation techniques for cartilage treatment and possible biological treatment in OA.

An Evidence-Based Approach to Orthobiologics for Tendon Disorders

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Andre Armando Abadin, Jordan Pearl Orr, Alexander Raphael Lloyd, Phillip Troy Henning, and Adam Pourcho

Tendinopathy is a chronic injury that affects both the athletic and general population. Recalcitrant tendinopathy is both frustrating for patients and providers once typical conservative treatments have been exhausted. Current research in orthobiologics shows that they are safe and could improve pain and function in recalcitrant cases. Unfortunately, many studies show inconsistency in the content of the orthobiologic injectate and approach in treatment protocols. There are robust data to support the use of platelet-rich plasma for the treatment of recalcitrant common extensor tendinopathy and plantar fasciopathy, but high-quality random control trials are needed before drawing definitive conclusions for other tendinopathies.

Protocols and Techniques for Orthobiologic Procedures

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Michael Khadavi, Adam Pourcho, and Luga Podesta

Many procedural techniques have been described and used for orthobiologic procedures with little research on the ideal technique. This section

outlines the commonly used materials and techniques from start to finish for these procedures. Post-procedure pain is common during and after many of these injections, and local and regional anesthesia during these procedures is discussed. Accuracy and safety of tendon, ligament, cartilage, intra-osseous, and spinal orthobiologic procedures are improved with the utilization of image guidance.

Intradiscal Leukocyte Rich Platelet Rich Plasma for Degenerative Disc Disease 117

Gregory E. Lutz

If we could choose a single non-fatal medical condition to find a better solution that would make the greatest impact on global health it would be a solution for degenerative disc disease (DDD) - the number one cause of chronic low back pain (CLBP).

Orthobiologic Treatment of Ligament Injuries 135

Luga Podesta, Eric S. Honbo, Raymond Mattfeld, and Michael Khadavi

Ligament injuries are common causes of joint pain, dysfunction, and disability resulting in disruption of joint homeostasis. Ligament injuries have historically been treated surgically. The autologous orthobiologic preparation used for treatment can influence the varying results reported. Therefore, to truly understand and compare results of these powerful therapies, reporting standardization, such as harvesting techniques, concentration techniques, quantification of the delivered product (platelets, progenitor cells), formulations (leukocyte content), number of injections performed, activation, injection technique (guided vs unguided), in addition to the post treatment rehabilitation process, are all important and necessary to evaluate and compare efficacy of future studies.

Prolotherapy: A Narrative Review of Mechanisms, Techniques, and Protocols, and Evidence for Common Musculoskeletal Conditions 165

Connie Hsu, Kevin Vu, and Joanne Borg-Stein

Prolotherapy is a nonsurgical regenerative technique that allows small amounts of irritant solution to be injected into the site of painful tendon and ligament insertions to promote the growth of healthy cells and tissues. The goal of prolotherapy is to stimulate growth factors that may strengthen attachments and reduce pain. Prolotherapy injection technique is centered around a focused physical examination and strong anatomic knowledge for maximized results. Prolotherapy is beneficial in a variety of different musculoskeletal conditions, including, but not limited to, lateral epicondylitis, rotator cuff tendinopathy, plantar fasciitis, Achilles tendinopathy, osteoarthritis, low back pain, sacroiliac joint pain, and TMJ laxity.

Orthobiologic Interventions for Muscle Injuries 181

Philip M. Stephens, Ryan P. Nussbaum, and Kentaro Onishi

Muscle injuries represent a common problem in active populations. Orthobiologics continue to be studied for their ability to improve muscle healing. To date, the basic science research for treating muscle injuries with platelet-rich plasma or stem cell remains novel. Furthermore, there are even fewer clinical studies on these topics, and their findings are inconclusive. Reviewing the literature, muscle injuries treated with ultrasound-

guided leukocyte-rich PRP injections appear to have the strongest evidence. Scar formation remains a major barrier in muscle injury healing, and there is optimism for future orthobiologic treatments that target the downregulation of TGF- β , resulting in decreased scar development.

Special Populations in Orthobiologics: Athletic, Elderly, and Pediatrics Populations 199

Arthur Jason De Luigi, Stephanie Tow, Ryan Flowers, and Andrew H. Gordon

This section is devoted to a review of the literature regarding the usage of orthobiologics in the special populations of elite athletes, the elderly, and pediatrics. The prospect of these regenerative options is encouraging to help provide alternative options that may enhance recovery and healing of acute and degenerative pathologic conditions. The goal is to provide the readers an overview of the existing literature highlighting areas with growing research and others that are still lacking.

Clinical Rationale and Rehabilitation Guidelines for Post Biologic Therapy 239

Eric S. Honbo, Raymond Mattfeld, Michael Khadavi, and Luga Podesta

The use of orthobiologic modalities such as platelet-rich plasma in orthopedics and sports medicine to deliver high concentrations of naturally occurring biologically active growth factors and proteins to the site of injury is very promising and continues to evolve. Early protection and tissue-specific progressive loading are critical components to successful outcomes following orthobiologic intervention. Each tissue heals and responds differently. Ligament, tendon, muscle, and articular cartilage each have unique healing properties that require tissue-specific loading. The authors have found using a criteria-based loading and exercise progression guided by dynamic imaging when appropriate to further advance the goal-oriented rehabilitation program. Each patient and injured tissue are unique and require specific intervention and rehabilitation.

Orthobiologic Techniques for Surgical Augmentation 265

Kenneth M. Lin, Christopher S. Frey, Ran Atzmon, Kinsley Pierre, Monica S. Vel, and Seth L. Sherman

General awareness and clinical utilization of orthobiologic therapy has increased sharply in the recent years. Orthobiologics can be defined as “biological materials and substrates that promote bone, ligament, muscle, and tendon healing.” There are 3 major strategies by which orthobiologics are thought to augment tissue repair or native biologic potential: factor-based, cell-based, and biomechanical augmentation. The purpose of this review is to synthesize the recent literature on orthobiologic techniques for surgical augmentation, with focus on several key areas including meniscus repair, osteochondral grafting, and rotator cuff repair.

Regulatory Considerations of Orthobiologic Procedures 275

Kudo Jang, William A. Berrigan, and Ken Mautner

The injection of biologic products for musculoskeletal pathologies is an emerging and promising field; however, dubious and unsafe uses for these products are often marketed. The Food and Drug Administration (FDA) has determined the need for varying degrees of regulation for these products

for safety and efficacy. These regulations are frequently updated and federally enforced. As the regulatory landscape changes, clinicians using biologic products must stay informed to remain within the purview of the FDA. This article describes the current regulations of the most common products: platelet-rich plasma, bone marrow aspirate concentrate, adipose-derived products, and birth tissue products.

Orthobiologic Standardization and Clinical Outcome Measurement

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Joshua Martin and Gerard Malanga

There is a pressing need for the standardization of orthobiologics, considering the cellular components, concentrations, and methods of injections may vary wildly, currently without significant standards of care. There is a growing body of evidence that these factors matter significantly for patient outcomes, so it is imperative that orthobiologic constituents are measured and standardized. Cell counts may be performed for platelet-rich plasma and bone marrow aspirate-based injections, whereas adipose should have standardized processing techniques as cellular quantification is more difficult.

Regional Anesthesia for Orthobiologic Procedures

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Michael Khadavi, Danielle Rehor, Alex Roney, Luga Podesta, and David R. Smith

Peripheral nerve blocks (PNB) can lessen procedural pain and eliminate the known detrimental effects of our local anesthetics on our orthobiologic target tissues. Local nerve damage and local anesthetic systemic toxicity are risks of PNBs that can be minimized with meticulous injection technique and an understanding of why these complications can occur. Herein, several PNB techniques are described in an effort to enhance procedural safety, efficacy, and comfort.