

EDITORIAL

Regenerative Medicine: Ushering in a New Era in Pain Medicine

Regenerative medicine is defined by the National Institutes of Health as “the process of creating living, functional tissues to repair or replace tissue or organ function lost due to age, disease, damage or congenital defects” [1]. The regenerative potential of the human body has intrigued humankind for millennia, as reflected in the Greek myth of Prometheus [2,3]. Chained to a rock in Caucasus as punishment for giving fire to humans, Prometheus’s liver was fed on by an eagle during the day, only to regenerate overnight so that it could be fed on again the next day. In ancient Rome, hot needles were used to induce healing in soldiers with joint dislocations [4]. In the mid-20th century, proliferative therapy, also known as prolotherapy, was developed to treat musculoskeletal pain, whereby an irritant solution (e.g., dextrose) was injected into muscles and joints to promote healing [5].

In the current era, in vitro and animal models demonstrate the potential of various agents to promote tissue growth. For example, stem cells derived from periosteum, synovium, umbilical cord blood, placental, adipose, and embryonic tissues have been used in animal models to promote growth of cartilage, bone, and other connective tissues by producing factors known to promote tissue growth [6]. Human mesenchymal stem cells (MSCs), cultured alongside human nucleus pulposus cells, produce proteoglycans and glycosaminoglycans, which are integral components of a healthy intervertebral disc [7]. Bone marrow-derived MSCs introduced into live rabbit lumbar intervertebral discs migrate and engraft into the annulus fibrosis [7]. In addition to stem cells, in vitro and animal studies of platelet-rich plasma (PRP), which contains high concentrations of growth factors, have demonstrated that PRP initiates smooth muscle cell proliferation [8] and bone regeneration [9,10].

In humans, regenerative agents have been used to treat pain attributed to osteoarthritis [11], tendinopathy [12,13], and internal intervertebral disc disruption [14,15]. For example, in a prospective cohort study of bone marrow-derived MSCs injected into the intervertebral disc of patients with discogenic pain, clinically significant improvements in pain and function were observed at 3-year follow-up [14]. In addition, radiographic improvement in disc hydration and structure was observed in a subgroup of patients [14]. Similar improvements in pain and function have been observed following intervertebral injection of PRP [15].

Although the current literature is promising, focused research is needed to better understand how regenerative technologies can be used in the treatment of patients with painful conditions. More specifically, there is a need for ongoing in vitro and animal studies to better elucidate the cellular mechanisms by which regenerative agents lead to improvements in pain. There is also a need for ongoing clinical trials including randomized sham or placebo-controlled trials, comparative effectiveness studies, and assessments of the influence of regenerative treatments on health service utilization. As the intersection between regenerative medicine and pain medicine evolves, we would like to introduce a new discipline, rehabilitation and regenerative medicine, to support the innovative work of basic science and clinical investigators engaged in advancing the core knowledge of this emerging field.

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Teaching Cases to Promote Clinical Advancement in Pain Medicine

It is well known that everyday practice yields interesting observations and materials that may lead to new ideas, concepts, or new studies [1]. The case series in this issue of *Pain Medicine* reported by Dr. Yu Tian and colleagues, “Unconventional Facial Entry Points Confirmed Using 3D CT Reconstruction-Guided Stereotactic Approach to Radiofrequency Thermo-coagulation for the Treatment of Trigeminal Neuralgia: A Case Series,” with its clarity of text and illustrations, exemplifies such a scenario [2]. Their observation about the variability of anatomical structures related to trigeminal nerve interventions provides important new information that may help improve clinical practice in the treatment of trigeminal neuralgia. Although *Pain Medicine* generally does not publish case reports or case series, as stated in our Instructions to Authors, we do recognize that case studies may initiate further investigation of a concept or practice.

The rationale for *Pain Medicine* generally not publishing descriptions of interesting cases in the form of Case Reports is twofold: first, case reports and case series are inherently limited in scientific rigor, and consequently they are unlikely to change practice or be widely circulated through citations in high-impact scientific journals; second, the journal has text limitations that require selective consideration in deciding what reports can practically be published and will have an important impact on the field. As an option, *Pain Medicine* considers for publication cases that are sufficiently novel and interesting for its readership in brief communications in the form of Letters to the Editor. Very rarely, editors may decide that a case report/series is important, illustrative, interesting, topical, or transformative and will review and publish these early empiric communiques in the main body of *Pain Medicine*. In this issue, the case series by Yu Tian and