many people would not be alive today if the development process had been abandoned because of early failures.

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Regarding “Randomized trial and local biological effect of autologous platelets used as adjuvant therapy for chronic venous leg ulcers”

We read with the greatest interest the paper recently published by Senet et al (J Vasc Surg 2003;38:1342-8). We appreciated the very professional way used to assess the in vivo and in vitro capacity of platelet concentrates to enhance healing of chronic ulcers. However, their results are quite different from our own.

We have used platelet gel in clinical practice since 2000. Platelet gel is a semisolid product obtained by activating autologous platelet concentrates with an autologous thrombin precursor by recalcification of autologous plasma. We obtain autologous pla-telet concentrates under the limit of biological activity of platelet concentrates. We are confident that Senet and colleagues obtained negligible results in vivo and in vitro, in spite their highly professional experimental trial, while in our hands more than 85% of patients respond to treatment and the healing time is roughly halved.

We are confident that Senet and colleagues did not obtain noticeable results either in vivo or in vitro simply because they used platelet concentrates under the limit of biological activity of...
growth factors therein contained. Similarly, we are confident that if the experiments were repeated using higher platelet doses, their findings would completely differ. Finally, we wonder about the exceedingly broad spectrum of exclusion criteria. Many of our patients are elderly, are diabetic, may have coexisting diseases including rheumatic diseases, may have bone or tendon, or may have very limited mobility. Actually, it is these kinds of patients who can particularly benefit from treatment with platelet-derived growth factors.

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Reply

We thank Dr. Piero Borzini and colleagues for their interest in our article, and we want to answer to their remarks. Borzini et al discuss three points: (1) the platelet concentration of the product tested for its wound healing adjuvant effect and the quantity of platelets applied on the wound to treat, (2) the platelet product used for cutaneous wound healing, and (3) the choice of chronic cutaneous lesions to treat with a platelet adjuvant therapy. Concerning the first point, we applied a lower quantity of platelets than Borzini et al (10 vs 0.2-0.4 × 10 platelets/cm) from a preparation at 5 × 10 platelets/mL (vs 1-2 × 10/mL). We observed in vitro biological effects induced by platelet lysates, with a maximal effect observed at 10 platelets/mL on normal dermal fibroblasts. The observed effects concerned cell growth as well as stimulation by platelets of fibroblast cytokine production. The figure presents the fibroblast growth curves in the presence of three different platelet concentrations, 10 platelets/mL corresponding to 10% platelets in the letter of Borzini et al. The cell growth was tested by an MTT test as previously reported by others.

Concerning the second point, the platelet preparation is indeed a crucial point, as is discussed in our article. Borzini et al used a platelet gel obtained by thrombin activation of platelet-rich plasma. This kind of preparation contains platelet growth factors and adhesive proteins but also lipid mediators and a fibrin matrix that mimics the matrix of the first steps of cutaneous wound healing.

Then, we arrive at the third point. Evaluation of the healing effect is the key point in clinical trials on wound healing. Many patients may improve with an adjuvant local treatment as a dressing, only because they are included in a trial, with good local wound care and adequate compression therapy. Thus, concerning venous ulcers, it is absolutely necessary to test therapeutic hypotheses in trials with a control group, and to take the rate and time to complete healing as endpoints of the study. Therefore, to obtain homogeneous comparable groups of patients, we excluded patients who presented with wounds that were not only from venous origin, such as patients with an uncontrolled systemic disease, as well as patients with bad local conditions such as bone exposition. It is important to emphasize that Stacey et al observed no platelet adjuvant effect for the closure of venous leg ulcers, using sonicated platelets in phosphate buffer saline at 3 × 10/cm. As discussed in our article, diabetic foot ulcers, but not venous leg ulcers, appear today to be good candidates for an adjuvant treatment with platelet products or recombinant growth factors. To our knowledge, no clinical trial has tested the therapeutic adjuvant effect of activated platelets in a fibrin gel for the closure of chronic cutaneous lesions.

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