With the increasing aging population, aged-related diseases are the big challenge in the 21st century. The aging organism can be considered to be in a prodromal stage, as it is only a matter of time for the first clinical symptoms to appear. Therefore, attempts to rejuvenate the aged body might not only provide us in future with “healthy aging” but might also be fundamental for therapeutic strategies to fight age-related diseases. A breakthrough for the field of rejuvenation was proof of concept experiments using an almost forgotten method, the parabiosis. Here, the blood circulation system of two individual animals gets fused, which provides a constant blood exchange between the two animals. Heterochronic parabiosis, i.e. fusing the blood system of an old with a young mouse, provided evidence that young blood rejuvenates the aged organism, for example muscle or brain tissue, and restores functions such as regeneration and learning and memory, which otherwise decline during aging. Thus, aging can be targeted through a systemic approach. Importantly, brain diseases such as Alzheimer’s dementia, which were previously considered as being isolated from the rest of the body, are now more and more seen as systemic diseases, which can be targeted through blood-borne factors or systemic approaches. Moreover, we might see age-related diseases with common mechanisms given that patients often come with co-morbidities, and a systemic rejuvenation approach might alleviate not only one but several symptoms.