# ТЕХНОЛОГИИ ВОССТАНОВИТЕЛЬНОЙ МЕДИЦИНЫ И МЕДИЦИНСКОЙ РЕАБИЛИТАЦИИ

### REHABILITATION MEDICINE AND MEDICAL REHABILITATION TECHNOLOGIES

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## THE EFFECTS OF BALNEOTHERAPY ON HUMAN IMMUNE GUNCTION: SHOULD BATHS AND MUD APPLICATIONS HAVE A ROLE DURING COVID-19 PANDEMIC?

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### **ABSTRACT**

Recent evidences show that balneotherapy applications can affect the immune system, which has an important role in the containment of Covid-19 infection outcomes. It is interesting to consider if balneotherapy, through medical water baths and mud applications can be a suitable treatment in order to influence human immunity in people who have not acquired the infection and in subjects discharged from hospital after Covid-19 recovery. In particular, balneotherapy seems to improve the immune response efficacy, with an effect mediated by mental stress reduction and a direct action, consisting in the modulation of the abnormal inflammation and the enhancement of the immune system, through changes in both cell-mediated and humoral immunity. The main changes demonstrated on human immunity, after balneotherapy, are linked to an increase in the levels and the activity of cells involved in the immune response such as neutrophils and monocytes and to a reduction of the pro-inflammatory cytokines produced by a dysregulated inflammation. Even if further in vitro researches and clinical trials on this topic should be conducted, at present Spa centres, if hygienically controlled according to WHO and national recommendations, may be considered safe places to attend and useful settings to counteract the outcomes of residual unbalanced immunity after Covid-19 infection.

**Keywords:** spa therapy; balneotherapy; hydrotherapy; mud therapy; immune system; immunity; Covid-19; cell-mediated immunity; humoral immunity; immunomodulation; rehabilitation; inflammation; spa environment; health.

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# ВОЗДЕЙСТВИЕ БАЛЬНОТЕРАПИИ НА ИММУННУЮ ФУНКЦИЮ ЧЕЛОВЕКА: ДОЛЖНЫ ЛИ ВАННЫ И ГРЯЗЕВЫЕ ПРОЦЕДУРЫ ИГРАТЬ ОПРЕДЕЛЕННУЮ РОЛЬ ВО ВРЕМЯ ПАНДЕМИИ COVID-19?

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### **РЕЗЮМЕ**

Последние данные показывают, что применение бальнеотерапии может повлиять на иммунную систему, которая играет важную роль в сдерживании последствий инфекции Covid-19. Интересно рассмотреть, может ли бальнеотерапия с помощью лечебных водяных ванн и грязевых процедур воздействовать на иммунитет людей, незаразившихся инфекцией, а также лиц, выписанных из больницы после выздоровления от Covid-19. В частности, бальнеотерапия повышает эффективность иммунного ответа, с эффектом, опосредованным снижением психического стресса и прямым действием, состоящим в модуляции аномального воспаления и укрепления иммунной системы, за счет изменения как клеточно-опосредованного, так и гуморального иммунитета. Основные изменения, демонстрируемые на иммунитете человека после бальнеотерапии, связаны с повышением уровня и активности клеток, участвующих в иммунном ответе, таких как нейтрофилы и моноциты, а также с уменьшением количества провоспалительных цитокинов, образующихся при дисрегулированном воспалении. Даже в случае проведения дальнейших лабораторных исследований и клинических испытаний на эту тему, в настоящее время СПА-центры при условии гигиенического контроля в соответствии с рекомендациями ВОЗ и национальными рекомендациями, могут считаться безопасным местом для посещения и полезными учреждениями для борьбы с последствиями остаточного дисбалансированного иммунитета после заражения Covid-19. Ключевые слова: санаторно-курортное лечение, бальнеотерапия, гидротерапия, грязелечение, иммунная система, иммунитет, Covid-19, клеточный иммунитет, гуморальный иммунитет, иммуномодуляция, реабилитация, воспаление, санаторно-курортная среда, здоровье.

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Nowadays world is facing Covid-19 pandemic, fighting a new and unexpected battle in which the immune system becomes one of the main weapons against the virus. Since human immune function has a significant role in order to contrast the infection and, even after the recovery, a persistent immune imbalance can lead to medium and long-term outcomes [1], we think it is interesting to consider if balneotherapy, one of the most used traditional and complementary therapies [2], can be a suitable treatment in order to influence human immunity in people who have not acquired the infection and in subjects discharged from hospital after Covid-19 recovery. Balneotherapy, in the form of mineral-rich water baths or mudbath therapy applications, has well-known positive effects in chronic musculoskeletal, dermatologic, and metabolic disorders. However, recent findings suggest that the effects of mineral-rich waters used in balneotherapy could also involve the immune system, improving the immune response efficacy.

First of all, it must be considered that the positive social atmosphere in which balneotherapy is carried out may have a beneficial effect on the immune system. In fact, a prolonged mental stress can damage human immune function through a systemic immunosuppression on both innate and adaptive immunity [3]. Thermal environment, relieving psychological concerns and mental stress, probably through a modulation of the neuroendocrine activity linked to an increase in systemic cortisol levels [4], can enhance the immune response.

Strong psychological stressors are associated with a reduced T lymphocytes and natural killer cells activity [3], important to contrast viruses. On the other side, it seems possible that after baths applications the concentration and the activity of CD8+ lymphocytes and natural killer cells may increase, probably depending on an enhanced somatotropic hormone production [5].

Even if there is a link between psychological sphere and immune response, balneotherapy can also have a direct effect on immunity. The mechanisms through which bathing in mineral-rich water or mud-bath applications may improve directly human immunity are still not fully understood. However, preclinical models have demonstrated at the cellular level that balneotherapy can have an anti-inflammatory and immunosuppressive role [6] and clinical trials have confirmed it. In an induced atopic dermatitis murine model, the serum levels of pro-inflammatory cytokines such as IL-1β, IL-13 and

TNF- $\alpha$  were significantly decreased after a treatment with high concentration mineral spring water [7]. Also in patients who underwent baths applications and mud therapy the inflammatory cytokines' activity seems to be modulate through an increase in anti-inflammatory IGF-1 as well as a reduction in serum levels of pro-inflammatory cytokines TNF- $\alpha$  and IL-1 $\beta$  [8, 9]. Furthermore, in patients with rheumatic diseases a reduction in the concentrations of prostaglandin E2 and leukotriene B4, significant inflammation mediators, was demonstrated after mud-bath applications [10] and C-reactive protein, which rise during inflammation, decreased significantly after balneotherapy applications [8].

Sulphur balneotherapy and mud-bath applications can also contribute to the balance between the pro– and the anti-inflammatory responses modifying the regulatory T cells proportion [9]. In particular, bathing in sulphur water can elevate the level of Foxp3+ Treg cells, which have an immunosuppressive activity [11].

Finally, thermal baths and mud-packs may also have a positive action on the oxidant/antioxidant system, with a reduction in the release of reactive oxygen (ROS) and nitrogen (RNS) species [10], contributing to an immunosuppressive action.

However, the effects produced by balneotherapy on human immunity are not only linked to an anti-inflammatory and immunosuppressive action, but they also seem to derive from an improvement of cell-mediated immunity. Radon bath applications can enhance cell-mediated immunity by giving a small but long-lasting increase in monocytes level [12], while sulphur water has been demonstrated in vitro to enhance the short-term survival capacity of neutrophils [13]. Furthermore, in patients with osteoarthritis, after hydrotherapy or mud-bath therapy an increase in neutrophils' functional capacity was demonstrated [8, 9], thanks to the influence of the previously mentioned rise in cortisol concentration [4].

Similarly, regarding humoral immunity balneotherapy not only has an anti-inflammatory role, but it can also lead to improve immune response. In fact, a higher concentration of IgA and C4 complement component, a vital protein that takes part in the clearance of antigen-antibody immune complexes, was demonstrated after 3 weeks of balneotherapy [14].

A complex balneotherapy intervention can also contribute to normalize lower level of immunity with changes in both cellmediated and humoral immunity. Struk et al. demonstrated that in patients who normalized their immunity after a complex mineral-rich water treatment neutrophils bactericidity and monocytes level increased, and also humoral immunity, through a rise in IgG levels, was enhanced [15].

In conclusion, there are several evidences that balneotherapy (through baths or mud applications) may reduce human dysregulated inflammation and enhance cell-mediated and humoral immunity. Further in vitro researches and clinical trials on this topic should be conducted in order

to better understand the mechanisms leading to these effects. Anyway, we think that at present Spa centres, if hygienically controlled according to WHO and national recommendations, with the application of stringent hygienic and disinfection procedures, may be considered safe places to attend by people without Covid-19 infection and useful settings to counteract the outcomes of residual unbalanced immunity after the recovery from Covid-19.

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