## SCIENTIFIC SESSIONS

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#### COVID-19

## COVID-19: SARS Cov2 TRANSMISSION ISSUES, CLINICAL PECULIARITIES OF LASTING SYMPTOMS

Yves Buisson (Académie Nationale de Médecine, France) - Lecture

#### **Generalities on Covid-19**

With more than 175,000,000 cases and 3,750,000 deaths, Covid-19 is the deadliest pandemic since the Spanish flu which hit the world at the end of the First World War in 1918-1919. This highly contagious respiratory infection is due to a beta-coronavirus called SARS-Cov-2, which appeared in China, in the city of Wuhan, province of Hubei, in December 2019.

In order to infect the host, SARS-CoV-2 must bind to a receptor present on the surface of cells, the Angiotensin-converting enzyme 2. ACE is an enzyme attached to the surface of cell membranes in vascular endothelia and various organs such as the heart, intestines, kidneys, etc. The first symptoms appear after an incubation period of 3 to 5 days, which can extend up to 14 days. Depending on the load of the viral inoculum and the physiological and sanitary state of the host, the disease can develop in 4 different clinical forms:

- asymptomatic in 30 % of cases, more frequent in young subjects,
- mild or moderate in 50 % of cases: it is an infection comparable to the flu (fever, asthenia, cough, headache, myalgia, arthralgia), with characteristic symptoms (anosmia, ageusia, diarrhea) which disappear after 2 to 6 weeks,
- severe in 15 % of cases: the disease is complicated by breathing difficulties which may lead to hospitalization,
- $\bullet$  critical in 5 % of cases: the disease progresses to acute respiratory distress or even multi-organ failure syndrome requiring intensive care and possibly leading to death.

It should be noted that in some recovering patients, symptoms may persist or reappear for weeks or months, even after mild illness. we will come back to this question in the second part of this presentation.

In severe forms, Covid-19 evolves in three successive phases: an early phase corresponding to viral replication, a pulmonary phase characterized by dyspnea, and a hyperinflammatory phase in which the intensity of the host's immune-inflammatory response determines the severity of the prognosis.

#### SARS-CoV-2 transmission

There are two ways in which SARS-CoV-2 can be transmitted: either directly from person to person through close contact or by droplets emitted when speaking, coughing or sneezing, or indirectly through aerosols or contacts with contaminated fomites. The main routes of propagation are direct transmission and airborne transmission.

Consequently, the three main preventive measures are:

- wearing a face mask, which must be generalized in public spaces to be effective,
- physical distancing between people, if possible of 2 meters,
- hand disinfection by washing with soap and water or by rubbing with hydroalcoholic gel. Droplets are large particles (at least 5  $\mu$ m) that fall quickly within 1 to 2 meters of the person emitting them. Aerosols are smaller in size, allowing them to stay suspended in the air for a few minutes to several hours, to travel distances of up to 7-8 meters, and to be inhaled.

SARS-CoV-2 is an enveloped virus that survives only a few hours to a few days at room temperature, with low relative humidity. It is quickly inactivated by detergents and disinfectants. It seems to be sensitive to solar radiation, especially to the action of UVC rays, which are artificial. The persistence of SARS-CoV-2 on surfaces varies according to the nature of the materials: a few hours on copper, latex and porous surfaces, a few days on stainless steels, plastics, glass and non-porous surfaces.

The stability of SARS-CoV-2 is higher at low temperatures and in the wet phase rather than in the dried form. Sars-Cov-2 can survive in water, but the risk of water contamination is extremely low when swimming due to the dilution of viral particles and the combined effect of pH, detergents, temperature and UV rays. It is found in environmental waters and sewers, but it appears to be quickly inactivated by physicochemical agents and does not present a risk of transmission. On the other hand, its quantification in wastewater is a good indicator of viral circulation in the source population. SARS-CoV-2 is inactivated by a wide variety of disinfectants that target the lipid layer of the envelope (for example, ethanol and detergents), or proteins of the envelope or capsid (for example, chlorine and glutaraldehyde), or nucleic acids (for example, chlorine).

Covid-19 lasting symptoms

From the end of the first epidemic wave in May 2020, the persistence of symptoms was described in more than 10 % of patients after 3 months and more than 60 % of patients discharged from hospital after 6 months.

Acute Covid-19 typically lasts for up to 4 weeks from the onset of symptoms. Post-acute Covid-19 is defined as persistent symptoms, or delayed or long-term complications beyond 4 weeks after the onset of the disease. The most common symptoms are:

- "general" signs: lasting pain, joint or muscle weaknesses or even extreme fatigue, headaches, respiratory discomfort, skin problems, anxiety, sleep disorders;
- disturbances or loss of smell and / or taste;
- renal, digestive, pulmonary or neurological complications.

In practice, there are two different situations: subacute or continuous symptomatic Covid-19, with symptoms present 4 to 12 weeks after the acute phase; and chronic or post-Covid-19 syndrome, with symptoms that persist or appear beyond 12 weeks after the onset of the disease and not attributable to other diagnoses.

The frequency and diversity of the prolonged or chronic forms of Covid-19 requires more multidisciplinary and coordinated outpatient management, starting with the

patients who have high risk factors, in particular severe acute Covid-19, stay in ICU, advanced age and comorbidities.

The Covid-19 has hurt us a lot, but it has also taught us a lot, and it is not over ...

#### **CLIMATOLOGY AND CORONAVIRUS. ARE THEY RELATED?**

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#### Introduction

The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic represents an unprecedented public health, social and economic problem. The role of seasonal and geographic climate variations in modulating the transmission of the virus has received increasing attention.

Knowledge of other viral respiratory diseases suggests that the transmission of SARS-CoV-2 could be modulated by seasonally varying environmental factors such as temperature and humidity.

The aim of this work is to review current literature on the effect of weather (temperature, humidity, precipitation, wind, cloudiness) and climate (temperature as an essential climate variable, solar radiation in the ultraviolet, sunshine duration) variables on SARS-CoV-2 and discuss their impact to the Covid-19 pandemic.

#### Methods

A search of electronic databases was conducted, including PubMed, Scielo, PEDro and Google Scholar from the year 2019 to the current date with the keywords: "climate", "factors", "SARS-CoV-2", "climatology", "weather".

Titles and abstracts were assessed for relevance to the question being studied. Articles references were further checked for inclusion of any potential missing articles.

#### Results

We selected 18 articles after duplicate removal, abstract screening and full-text eligibility assessment, from 44 articles identified through database searching.

The effect of weather and climate variables as well as of air pollution on Covid-19 was investigated using different approaches across diverse locations and time periods. It was found that ambient temperature, humidity and the number of newly confirmed cases were the most frequently used variables. It was also shown that Covid-19 seasonality is more pronounced at higher latitudes.

According to most of the studies, temperate warm and cold climates are more favourable to spread of the virus, whereas arid and tropical climates are less favourable. The majority of studies show that humidity has a reverse relationship within the virus outbreak speed and that solar radiation threats the virus's survival. In one study, however, the association between the weather variables and Covid-19 was not significant when

additional covariates related to social distance measuring were included in the analysis. Low wind speeds might enhance airborne transmission, according to the correlation found in several cities. Atmospheric pressure is a quite significant factor and could be one of the most related with the virus transmission. Daily sun hours and rainfall seem to be non-significant factors, although their contribution might be implicit in the mean temperature and also in the atmospheric pressure.

There is also a positive association between air pollution, urban environment and Covid-19 infectivity and mortality. Population density and intra-provincial movement have a direct relationship with the infection rate.

The significant increase in the number of cases suggests that SARS-CoV-2 is capable of producing outbreaks at high ambient temperatures such as during summertime period in Southern Europe (e.g. Spain, Greece, Bulgaria). These findings highlight that in the absence of public health measures climate conditions cannot mitigate SARS-CoV-2 outbreaks and that the seasonality of SARS-CoV-2 differs greatly compared to common cold coronaviruses or influenza. It has been shown that containment measures have a much stronger impact than the weather and climate variables.

#### Conclusions

Although the impact of weather and climate variables to the Covid-19 transmission rate seems likely, a solid conclusion on the degree of impact needs further investigation. Seasonality alone is not sufficient to curb the Covid-19 transmission. The effect of climate factors, in the absence of public health interventions cannot mitigate Covid-19. Key-words: "climatology", "weather factors", "SARS-CoV2"

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#### BALNEOLOGICAL TREATMENTS FOR POST-COVID FACT OR FICTION ?

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Keywords: Covid-19; balneology; spa therapy; health resort; rehabilitation

#### Introduction

There is limited evidence that the spa therapy with specific balneological treatments such as thermal or mineral water inhalation and oral-nasal irrigation can be effective in the convalescence periods after acute infectious diseases or in the chronic periods of some inflammatory or allergic conditions [Stier-Jarmer et al. 2015]. For example, in chronic respiratory diseases, complex spa therapy regimens (combination of balneological treatments and other therapeutic interventions) is used to a limited extent, being more common in some countries [Khaltaev et al. 2020]. During the Covid-19 pandemic if spa therapy might be beneficial in post-Covid patients with or without pulmonary involvement is being increasingly discussed. In search of existing evidence on therapeutic or rehabilitative potential of spa therapy in such cases we aimed to perform a narrative review.

#### Methods

We conducted a comprehensive literature search on the Google Scholar website using the search terms Covid-19, balneology, spa therapy, health resort and rehabilitation in the period of January 2020 and April 2021. Although Google Scholar is not without limitations, it offers a practical starting point for a more comprehensive literature search with no language restriction.

#### Results

We identified one uncontrolled observational study published in Russian [Efimenko et al. 2021]. We only included this clinical study for evaluation. We excluded five publications; 3 letters to editor, 2 reviews and 1 hypothesis article discussing the balneological or thermal or health resort treatments as potential interventions for the management of post Covid patients since they were based on suggestions and postulations.

The study of Efimenko et al, aimed to evaluate the efficacy of a rehabilitation program in a health resort facility located in Pyatigorsk in Russia. through the assessment of functional state of the cardiorespiratory system of 29 patients affected by the Covid-19 pneumonia [Efimenko et al. 2021], Patients underwent a two-week spa therapy program consisting of drinking mineral water, forest therapy (terrain cure), exercise therapy, mechanotherapy, halotherapy, normobaric oxygenation, chest massage and inhalations. After such a complex spa (thermal) therapy course patients have shown increase in the

general adaptive potential and exercise tolerance.

#### Discussion

Despite the attempts to determine the role of health resort medicine in combat with Covid-19 pandemic only one observational study tested a two-week complex spa treatment, patients affected by the Covid-19 pneumonia yielding positive results such as decrease of vegetative imbalance and increase of tolerance of cardiorespiratory system to physical loads. Authors stated that these beneficial effects were due to "sanogenetic", "adaptogenic" effects of the applied interventions on regulatory systems of various levels of biological integration [Efimenko et al 2021].

First step should be to determine which balneological agent (for example which mineral water; saline, sulfurous etc.), which balneological treatment (such as bathing, drinking or inhalation) or balneological treatment combinations could be effective. Additional treatments (e.g. exercises, health education, nutrition, etc.) could be added or integrated into the spa therapy program which will be applied in a thermal (spa) resort [Karagülle and Karagülle 2021].

The next step will be to test this possible spa treatment regimen at an appropriate spa facility in a well-defined Covid-19 patient group in a randomized controlled clinical trial. Furthermore multicenter studies with larger patient groups would be carried out in more than one spa facility in order to verify the effectiveness of well-defined complex spa therapy regimens in post-Covid cases.

#### Conclusion

Considering the high number of people affected by Covid-19 infection worldwide, spa therapy regimens with balneological treatments for post Covid patients seem to play an important role in countries where they are available and included in health care systems. But very scarce evidence implies that spa therapy may be considered as a therapeutic or rehabilitative measure for post-Covid cases who had pneumonia. There is an urgent need for well-designed randomized controlled studies testing the efficacy of various spa therapy regimens after Coronavirus infection.

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## COVID-19: SPA THERAPY FOR PATIENTS WITH LONG-LASTING SYMPTOMS

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The UK's National Institute for Health and Care Excellence (NICE) proposes to divide Covid-19 disease into three phases :

- Covid-19 with symptoms: can occur up to 4 weeks after infection with SARS-CoV-2.
- Ongoing symptomatic Covid-19: occurring between 4 and 12 weeks.
- Post-Covid-19 Syndrome : the effects of which may last beyond 12 weeks.

According to the proposed definition, the terminology long Covid include the last two phases (Covid-19 with prolonged symptoms + post-Covid-19 syndrome) to define the persistence (or development) of sequelae after Covid-19 with symptoms.

Considering the role it already assumes in the field of re-education/rehabilitation, spa medicine is well adapted to the management of patients suffering from long term Covid, and brings an answer to these patients with a mild form of Covid suffering from persistent symptoms, as well as to those who recover with difficulty from a more severe form and whose health condition is compatible with a thermal stay.

The long Covid thermal care programme constitutes a new intervention, which, in addition to thermal care, combines rehabilitation practices and services which feature a new type of care in all respects (medical, organisational, administrative and financial).

#### Target population

Patients with the following pathologies constituting severe sequelae are contraindicated:

- pulmonary fibrosis,
- myopericarditis,
- pulmonary embolism, cardiac ischaemia, stroke and vascular complications,
- severe depressive syndrome in progress, delirious decompensation or a state of panic attacks comorbid with PTSD.

In addition, the programme is inadvisable to patients who are desaturated during exercise or who require oxygen therapy for exercise.

#### Intervention

The general objective of the intervention is, in patients without respiratory, cardiac or neuro-motor sequelae, to regain the level of independence that they had before the disease

At the end of the treatment in a thermal environment, the patient must:

- i) have recovered as much as possible over a period of 3 weeks,
- ii) have acquired the cognitive and sensory-motor skills that will enable them to

continue their care after returning home.

iii) have become aware of his or her capacity for progress, mainly on the basis of the progress made during the thermal stay.

The intervention is based on four pillars:

- hydrothermal treatments: individual balneotherapy, heat, mud or other, massages, mobilisation pool will bring all patients the benefit of their analgesic, sedative, muscle relaxant and anxiolytic actions, and their facilitating effect on movement and static and dynamic balance.
- acquisition of ventilation control,
- strengthening of the musculature and good balance,
- exercise training.

Depending on the needs of the patients, care can be completed to treat possible persistent sensory problems (smell).

#### Assessment

An appropriate assessment using validated and shared tests is the essential prerequisite for starting the intervention but also for continuing it and adapting it to the patient's tolerance and progress. It is a matter of identifying and quantifying, whenever possible, by means of appropriate assessments, the problems requiring therapeutic intervention, mainly respiratory phenomena, pain, fatigue, loss of muscles and/or strength, balance problems, dysautonomia, somatic functional disorders, sensory problems, etc.

The assessments must use validated, relevant, simple scales that can be understood by the patient, who must be able to perceive the benefits of the intervention both by the elements felt and by the objective modifications of the rated assessments carried out. Scales will include the ADL scale (level of functional independence), Chalder scale and Borg questionnaire (fatigue), Nijmegen test (respiratory test), sit-to-stand test and sixminute walk test (locomotor condition), HAD (psychological status),...

The spa doctor examines the patient and undertakes the assessment that corresponds to the patient's particular situation. Following this assessment, he prescribes the spa treatments and determines the necessary complementary interventions among those proposed. It is at this moment that the therapeutic contract with the patient is drawn up, a real contract of objectives and means which commit both parties.

This assessment will be completed by specific assessments, in particular by the physiotherapist, dietician, nurse, sports educator, psychologist, etc. Quantified assessment should be repeated. Progress, however small, should be used to reassure the patient about his or her future and also to determine the self-help activities to be continued at home. Verification of skill acquisition is also essential, to ensure that the patient has mastered the tools to be their own therapist, at least for the most part. It is also a good idea to maintain contact with the patient to find out about his or her condition, progress, difficulties, etc., whether or not results have been achieved, and to renegotiate the contract of objectives and means, if necessary.

#### **Doctor's prescription**

The post-Covid spa programme consists of a 3-week spa treatment supplemented by rehabilitation activities.

Its implementation requires the simultaneous prescription by the doctor of a request for spa treatment and a request for coverage of the post-Covid spa programme.

The financing of the programme is under discussion with the National Health Insurance Fund.

The cost of the spa treatment should be covered according to the usual conventional rates and conditions (usually 65 % of the cost). Coverage of the post-Covid thermal programme could benefit from a specific rate, not yet defined.

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#### **BIOTHERAPIES AND RISK OF SEVERE FORMS OF COVID-19**

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Keywords: Covid-19, bDMARDs, tsDMARDs, anti-CD20, corticosteroids

#### Introduction

Biologic Disease Modifying Anti-Rheumatic Drugs (bDMARDs) with tumor necrosis factor alpha inhibitors, interleukins 1, 2-13, 6 or 17 inhibitors, anti-CD20 and anti-CD 28 treatments, and targeted synthetic Disease Modifying Anti-Rheumatic Drugs (tsDMARDs) with janus kinase inhibitors have improved the prognosis of many chronic inflammatory pathologies in rheumatology but also in gastroenterology (especially inflammatory bowel diseases (IBD)), dermatology (psoriasis) and neurology (multiple sclerosis). They act on the processes involved in inflammation, modify the immune response and the response to infections. More and more patients, and therefore spa patients, are being treated with these treatments. The context of a spa treatments is likely to expose to a risk of Covid-19 infection due to the promiscuity between patients. Consenquently, it appears useful to specify whether the risk of Covid-19 infection is more frequent and/or more severe in patients treated with bDMARDs and tsDMARDs and if so whether it is necessary to contraindicate spa treatments to them.

#### Methodology

We carried out a bibliographic search on the Medline and Embase databases using the keywords "Covid-19", "bDMARDs" and "tsDMARDs" in order to identify the studies evaluating the risks of Covid-19 infection in patients treated with bDMARDs and tsDMARDs. We then investigated whether these patients had a greater frequency and severity of Covid-19 infection.

#### Results

We found 15 studies comparing the prevalence and/or severity of Covid-19 infection in a population of patients treated with bDMARDs or tsDMARDs versus an untreated control population. These were patients with chronic inflammatory rheumatism (9 studies), IBD (1 study), IBD or chronic inflammatory rheumatism (1 study), psoriasis (2 studies) and multiple sclerosis (1 study).

Two studies showed an increase in the frequency of Covid-19 infections but without an increase in severe forms in the population treated with bDMARS or tsDMARDs. However ten other studies did not show this increased in the frequency of infections.

Three studies showed a significant increase in severe forms of Covid-19 (defined by hospitalization in intensive care unit or death) in patients specifically treated with anti-CD20 (rituximab, ocrelizumab)

Eight studies have shown an increase in severe forms (requiring hospitalization) in patients treated with corticosteroid therapy. The results of the studies diverge on the posology of cortisone at which the increased risk of the severity of the infection appears.

In most studies the risk factor associated with severe forms of Covid-19 (defined by hospitalization or death) are age, male sex and comorbidities (overweight, diabetes, arterial hypertension, heart disease).

#### Conclusion

Anti-CD20 treatments (rituximab, ocrelizumab) and systemic corticosteroids appears to increase the risk of severe Covid-19 infection. Other bDMARDs or tsDMARDs does not appear to increase the risk of severe Covid -19 infection. Due to the risks of Covid-19 infection linked to promiscuity between patients, the contraindication of spa therapy should be discussed in patients treated with high-dose corticosteroid therapy and/or anti-CD20 treatments.

#### SPA TREATMENTS FOR STRESS RELATED SYMPTOMS OF COVID 19

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The exceptional global situation that we have been experiencing for the past 18 months in the context of the Covid-19 pandemic is causing a major psychological imbalance throughout society. For the first time in history, a pandemic is having societal repercussions that affect all individuals on all continents. The extensive media coverage of this pandemic has also contributed to this global psychological trauma. For the past 18 months, the major psychological repercussions have been accumulating. It is considered that the international prevalence of mental illness has tripled since the pandemic. This situation is strongly reminiscent of post-traumatic stress as defined in the DSM-5. We propose here to revisit this pathology in order to make the link with what most of the

subjects who suffer from it experience. What are the specificities of post-traumatic stress and what differentiates it from a major depressive state, not incompatible with PTSD? What are the risk factors that favour this type of decompensation? What are the psychopathological mechanisms of these induced psychotraumatic reactions? We recall here some results of international studies or surveys carried out and published in various French, European or American journals. We then present the most recommended therapeutic and preventive strategies to fight against PTSD and which can perfectly be set up within the framework of spa stays. Spa resorts centres are privileged therapeutic places to ensure such objectives. Why is this therapy particularly interesting for such treatments? Because these psychic decompensations are induced by environmental factors, and are improved by them. Thermal spas can create an environment which favours the regression of the reactive psychic symptoms. We present here a specific model of support for traumatised patients by Covid-19, based on 4 modules on understanding the coping mechanisms, managing fears, identifying resources and resilience capacities, and ways of regaining positive feelings. We also present here the feedback from the year 2020 at the Saujon Thermal Stress School, which provides valuable information on the effectiveness of this therapeutic approach in psychosomatic spas.

#### MENTAL HEALTH AND COVID-19 - THE ROLE OF BALNEOTHERAPY

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Keywords: Mental Health; Covid-19, Balneotherapy

#### Introduction

During the Covid-19 pandemic, several studies showed the consequences of SARS-CoV-2 infection on mental health. The measures implemented by the governments of the various countries had a significant impact due to lifestyle changes. Balneotherapy is known for its beneficial effects in terms of physical and psychological well-being.

#### **Objectives**

To know what has been published regarding the effects of balneotherapy in mental health. According to the results, to stablish a possible balneotherapy protocol in order to start a pilot study on this issue.

#### Methods

Literature review, searched on Pubmed and Google Search, using the terms "mental health and Covid-19", "mental health and balneotherapy", and "mental health, balneotherapy, and Covid-19". Our review was limited to the articles published in the previous 5 years and concerning adult individuals.

#### Results

A total of twelve articles were included and analysed. Five articles corroborated the increase of anxiety, depression, insomnia, and stress in response to the Covid-19 pandemic. Some authors emphasized that mental illnesses that arise in this context may be, in more extreme cases, similar to post-traumatic stress syndrome. We found seven articles reporting the beneficial effects of balneotherapy in reducing anxiety, stress, depression, fatigue, and one of them reporting the reduction in cortisol with this type of treatment.

#### Conclusion

There are reports of beneficial effects of balneotherapy on quality of life and mental health with few adverse effects, compared to pharmacological therapy. According to the results, we decided to create a protocol for balneotherapy that includes observation by the Family Physician/Hospital Physician who, after applying the reduced profile of mood states scale and according to the obtained result and in the absence of contraindications, refers the patients to Thermal Establishments. Here, the Hydrologist Physician prescribes the treatment according to the needs of each patient, for a period between 12 to 21 days. This procedure will be first tested by a pilot study and later on, we will consider to progress on this clinical investigation through of controlled trials.

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## REHABILITATION CENTER AS A TEMPORARY COVID HOSPITAL OUR EXPERIENCES

#### Jokiç Aleksandar, Serbia

Key words: covid-19, rehabilitation

#### Introduction

Specialized rehabilitation hospital Banja Koviljaca is one of the oldest and biggest rehabilitation centers in Serbia (founded in 1858), however due to sudden increase in number of covid19-positive patients, it became a temporary covid hospital, by the order of Ministry of Health of the Republic of Serbia.

#### Methods

Research was conducted from November 2020 till January 2021.

#### Results

We have treated a total of 213 covid positive patients, 65 % of whom were males. The average treatment duration was 15 days. 22 % of the patients suffered from diabetus mellitus, 67 % had a cadiivascular disease, 5 % had a malignant tumor, and 24 % had comorbidity. 54 % had elevated d-dimer. 61 % of them had supplemental oxygen. 91 % were taking cotiicosteroids. 95 % had pneumonia, and 86 % had bilateral pneumonia. All of them received anibiotics, and 9 % received anti-virus therapy. 33 of them were transferred to another treatment facility due to aggravating conditions, and we only had one fatality.

#### Conclusion

Even during the pandemic of an infectious disease, a rehabilitation center has a significant place in the healtcare system of a country.

## CHALLENGES BEFORE BALNEOLOGY IN BULGARIA IN A PERIOD OF COVID 19

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The world was completely unprepared for addressing the serious health threat the infection of Covid-19 is. Expectedly, the individual health systems reacted differently to this challenge. However, one commonality is often observed that is patients with chronic diseases became victim of the anti-Covid-19 measures. The attention is concentrated in fighting the pandemic, which is at the expense of the medical care for the above-mentioned group of patients with chronic musculoskeletal diseases, incl. reumatological diseases, diseases of the central and peripheral neural systems, as well as of the respiratory and excretory systems, among others.

In the period of accommodating knowledge about the infection and thus, how to address it the pandemic, professionals in the Bulgarian balneotherapeuticals centres defined the following challenges:

- 1. What are the best anti-epidemic measures and how should we apply them in order to avoid spreading the infection among staff and patients in balneotherapeuticals centres.
- 2. How to organise the rehabilitation of patients in the post-Covid-19 phase with maximum positive effect for the recovery from the infection?
- 3. How to organise the balneo-treatment of all patients, incl. of those with chronic diseases?

During the period of 13.03.-1.06.2020, when the Bulgarian state introduced a state of emergency and the first anti-Covid-19 measures, hospitals for rehabilitation and medical spa centres were closed down. Their staff members used the opportunity to draw anti-epidemic plans and to get prepared for their future work under the conditions of Covid-19 pandemic with post-Covid-19 patients who need medical care and rehabilitation for their recovery. During the following periods of stricter restrictions hospitals for rehabilitation and medical spa centres were allowed to open under the condition of severely restricted capacity.

The post-Covid-19 syndrome in its multiple manifestations created the need for formation of rehabilitation algorithms for the patients. The more we learned about the infection, the more we realised that it has specifics, which have to be taken into account. They are related to predilection place of the inflammation and the post-Covid syndrome

and the variety of symptoms during the period of recovery.

With time, one of the most significant problems with Covid-19 that we in Bulgaria are facing is the very high death rate. One of the explanations is the fact the country is at the top of the list of people suffering from cardiovascular and cerebrovascular diseases in Europe. This very worrisome trend raises the question of prevention and prophylaxis of some chronic diseases. This is yet another challenge for balneology - to become part of the active prophylaxis of vascular pathology and other diseases of social significance - all of them risk factors for Covid-19 with severe complications.

In the last decades balneology was neglected due to the unjustified perception that pharmacy can be an effective substitute. The positive effects of the natural healing factors lie not only in the limited local impact of mineral water and healing mud, but also in the benefits of a complex and overall treatment that takes place in a resort, whose climate, mineral waters and healing mud help the recovery of the human body and mind, as well as improve the immune protection and the resilience against viruses and bacterial infections

The presentation will include data on the medical treatments performed in the Hospital, Specialised for Rehabilitation and Medical spa center in Hotel Strimon Spa Garden in the city of Kyustendil, for the period of 2019-2020.

## COVID 19 AND THERMAL CARE FACILITIES IN FRANCE : 2020 EXPERIENCE, 2021 PROJECTS

#### C-E. Bouvier, L. Dorothée, T. Dubois (France)

In front of the increasing dissemination of the SARS-CoV-2, the Conseil National des Etablissements Thermaux (Cneth) took the initiative to create, as soon as February 27th, 2020, a multi-stakeholders cell of prevention and crisis management, by associating the representatives of the thermal operators and of the thermal towns, doctors, the Institut du Thermalisme, quality experts and two infectiologists. Thereafter, thanks to a fluid cooperation of the stakeholders, the unit produced a sanitary reference frame which identifies 96 measures to be applied to allow the reopening of the spa establishments. This reference frame was validated by the Health Ministry on May 29th, allowing for an early reopening on the date of 2 June.

The following were considered as prerequisites prior to the opening:

- 1° the establishment within each spa resort of a Covid-19 coordination structure, identifying in particular a Covid-19 referent,
- 2° the regulatory and technical provisions relating to the sanitary control of sources and points of use (in particular the adjustment of automatic chlorination treatment systems) and to maintenance operations (cleaning/disinfection, ventilation/air conditioning systems),
- 3° prior training of all personnel in the prevention and management of Covid-19 risks,

according to a training programme outline drawn up by the Cneth,

- 4° the creation of a zoning plan distinguishing dry/wet areas, necessary equipements and determining the Maximum Instantaneous Attendance or gauge of the facility,
- 5° the development of the plan for wearing personal protective equipment (PPE): the crisis unit discussed the wearing of masks at length, given the limitations imposed, both in terms of ergonomics and respiratory comfort, and the level of performance in a hot and humid environment,
- 6° the procedures for dealing with possible cases and positive cases (isolation procedure, RT-PCR test, suspension or interruption of the treatment, possible hospital treatment).

These prerequisites are accompanied by measures which apply in the operational phase of the establishments. We can distinguish schematically the measures which are common to establishments receiving the public and those which are specific to thermal establishments.

Among the measures specific to thermal establishments, the following have been identified:

- a systematic diagnosis to look for signs suggestive of Covid-19 was completed by each curist before the start of treatments.
- the adaptation of certain treatment units to allow the respect of the rules of spatial distancing (at least 1 m on all sides between two curists). When the configuration of the installations does not allow it, the operator has organised the spacing between the patients, either by partitioning the treatment stations (ENT stations, collective basins, steam rooms, manudouches, etc.), or by leaving a treatment station vacant between two occupied treatment stations.
- the re-evaluation of the protocol of certain treatments: for thermal pools, the prevailing rule is that of 1 bather for 2 m<sup>2</sup>. In addition, the physical distance of 1 m between the bathers was observed or a physical screen allowed their separation.
- heating the thermal mud used in some treatment programmes to 70°C for 30 minutes to inactivate SARS-CoV-2 before use.
- suspension of collective care that potentiates the spread of the virus : spray/aerosolisation care for all patients and in all orientations.

#### Assessment of the 2020 season

191,000 curists were welcomed in 2020 (i.e. a drop in attendance of -67 %), of which 180,000 were taken care of during the period subject to the application of the health protocol. Less than thirty cases of Covid were reported, that is to say an incidence very largely lower than that recorded in the general population. Moreover, the contact tracing procedure did not reveal any outbreaks. Subsequently, no severe cases were reported. Only one case required a collective RT-PCR screening operation carried out by the Regional Health Agency (ARS), involving 446 people: 135 staff members and 309 curists. Among the 135 staff members, 2 asymptomatic employees turned out to be "doubtful". After a second test 48 hours later, the 2 people proved to be negative. Among

the 309 curists, 7 were positive, including 5 asymptomatic ones (65 %), who did not show signs likely to favour the diffusion because they were asymptomatic. In agreement with the Regional Health Agency, no closure of the establishment, nor even of the service was required. It is therefore legitimate to conclude that the measures decided upon and rigorously applied by the spa operators have borne fruit and that the approach has proved its efficiency.

#### Adaptation of the provisions for the 2021 season

The reopening of the thermal establishments in 2021 has required the adaptation of the sanitary reference frame, thanks to the better knowledge of the virus circulation modes, to the evolution of the screening techniques, to the shortening of the delays of obtaining the results, and to the massive vaccination of the population. At the time of writing, the following changes are being considered in particular:

- the access to the thermal establishment could be conditioned to the production of a negative result of an RT-PCR test of less than 72 hours. The curists with a full vaccination scheme (usually a double vaccination) will be exempted from the production of such a test
- the wearing of a mask for the general public with a filtration rate greater than 90 % (corresponding to the so-called "category 1" mask), or a surgical mask,
- compliance with the physical distance introduced by the new National Enterprise Protocol of 16 February 2021 requiring a distance of 2m between two people when the mask cannot be worn,
- emphasis on the ventilation/air renewal.

# The impact of the COVID 19 pandemia on the functioning of thermal treatment in Poland - medical, economic and social aspect

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Keywords: Thermal center in Poland; Pandemia COVID19

The first case of a patient with SARS COV2 in Poland was diagnosed on March 4, 2020. On March 23, by the decision of the Minister of Health, health resorts in Poland was closed. The first break lasted until June 15, 2020. In the following months, the spa treatment carried out treatment and rehabilitation in a sanitary regime with the number of patients reduced to 50 %. In the period from October 24, 2020 to March 11, 2021, a ban on spa activities was again introduced. Since March 11, so far, spas in Poland are again operating in a sanitary regime analogous to summer 2020.

The restrictions introduced as a result of the pandemic resulted in:

#### Medical problems

- 1. Problems with accessing services for patients with chronic diseases (70 % fewer patients benefited from the treatment than in the previous year
- 2. A delay in obtaining rehabilitation worsens the results of treatment in cardiological, neurological, rheumatological, metabolic and other patients.
- 3. Patients with chronic diseases, previously treated in health resorts, more often required inpatient hospital care. Getting this help was very difficult due to the transformation of many hospitals into an infectious hospital for patients with Covid.

#### **Economic problems**

- 1. Despite the implementation of protective programs, most thermal center facilities recorded significant financial losses, about 10-15% of entities had to close their activities
- 2. Most of the hotels, restaurants and retail outlets in thermal cities found themselves in a critical situation.
- 3. To protect jobs, most thermal centers workers experienced a significant reduction in income.
- 4. The opening of the spas in March 2021 did not improve the situation due to the reduced number of patients and increased costs of the sanitary regime. Thermal centers continue to suffer losses.

#### Social problems

- 1. Qualified medical staff: doctors, nurses, physiotherapists, psychologists and dieticians were forced to look for alternative employment. Many now work in Covid hospitals. This resulted in huge staff shortages in many spas. Rebuilding the medical staff requires a long period of time
- 2. The queues of people waiting for refunded spa treatment have become very much longer. Many people in need of help give up treatment
- 3. Lack of work in health resorts forces residents of health resorts to emigrate for work to other centers.

Despite these and many other problems, which will be discussed in the presentation, more than 80 % of spa facilities have started their activity at the moment. The increasing number of vaccinated elderly people is conducive to the safe conduct of spa treatment in a large part of the population. In addition, a rehabilitation program after a Covid-19 incident was implemented in Poland. Spa facilities have been involved in this program to a large extent. The experience of the year of the pandemic allowed for the preparation of guidelines for the management of spa treatment, which currently almost 100 % protect against the emergence of viral transmission outbreaks.

It seems that even in the case of a further increase in the number of Covid-19 patients, health resorts in Poland will not be closed again. The number of new cases of SARS-COV 2 infection in spa towns during the periods of approval for their operation was not

higher than the population average. Spa treatment in Poland currently has a very important role to play in reducing the health effects of the pandemic, both in people who have complications after infection with SARS-COV2 as well as in people with chronic diseases and whose health has deteriorated. I will present the principles of health resorts operation in Poland after the pandemic at the end of my presentation.

#### **MUDS**

## AN OVERVIEW OF THE USES OF THERMAL MUD IN FRENCH THERMALISM

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Key words: thermal mud / pelotherapy / uses / evolutions

The AFTh brings together specialists with a scientific and academic interest in thermal techniques. Engineers, technicians, managers, suppliers, manufacturers, design offices, and scientists meet in congress every year in a thermal town around a topical theme linked to the use of hydrothermal techniques.

Each year, an initiative prize rewards a technical achievement or a project likely to improve the quality, ergonomics, economy, and efficiency of a thermal spa centre.

#### Introduction

In France, unlike natural mineral water, there are no regulations for the sanitary control of thermal mud. The Good Practices guide for the French thermal spas has some requirements regarding quality and the sanitary conditions of thermal muds uses.

Due to the various therapeutic uses of these thermal muds, their mode of administration and the state of health of the exposed populations, it appeared necessary to provide an overview of the use of these thermal muds and the safety requirements regarding the state of health of the exposed populations.

#### Method

This study is based on a survey among the 90 members of Cneth (National Concil of Thermal Centres).

More than half of the members responded to the survey conducted in 2013 based on a form sent by email and conducing the same survey than the one conducted in 2004.

The questions focused on the types of thermal muds used for each therapeutic indication, the substrates used, the modes of dispensing this treatment (illutation *vs* poultice), the modes of manufacture (extemporaneous *vs* matured) the uses (recycled *vs* single use) and the characteristics uses (weight, temperature, etc.). This questionnaire continues with a question about the destination of this derivative and finally ends with a question about the improvements made by the thermal spa centres and the associated investments.

#### Results

The comparison of the responses (2013 vs 2004) highlight the following points: The thermal muds remain mainly used in HR orientation (Rheumatology). The illutations seem to be used more than previously with in parallel a reduction in poultices.

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The extemporaneous mud is mainly used (at 68 %), mainly made from clay in the form of a poultice while the matured sludge is mainly used in illutation.

In poultices, personalized use remains predominant even if single use is on the rise. The operating temperatures are mainly between 40 and 45°C (the average temperature having fallen compared to 2004). Likewise, for the illutations the temperatures used are colder (between 35 and 50°C) and the average weight of the mud used has also fallen (1kg for the general and -0.5 kg for the local).

The destination of muds, as waste, is a significant financial burden for Centers. Indeed, 66 % of the stations questioned send their used sludge to waste reception centers and 14 % note an increase in these reprocessing costs. On the other hand, 34 % of the stations questioned have set up a recycling process for these derivatives which are then "regenerated" by pasteurization.

Half of the thermal centres that responded to the survey declared having made investments in the mud process in the last 10 years with modifications of the process and / or the purchase of specific equipment such as heating cabinets (individual use) or mixers.

We can note the particular case of the thermal baths of Balaruc which have developed a new type of application in the form of "diffusion beds" using a liquid mud (72.8 % natural mineral water) based on clay . This mud, recovered at each application is pasteurized before reuse. Increasing the volume of thermal water in the peloid would increase the therapeutic effectiveness of the application by combining the richness of trace elements with the benefits of constant heat (42°C) throughout the treatment. The Balaruc-les Bains thermal mud network was the subject of the AFTh prize in 2015.

#### Conclusion

The most significant changes over the past 10 years were in the supply, manufacture, and sanitary control of this thermal derivative and the corresponding update of the Good Practices guide for the French thermal centres (GBPTh) developed at the request of the Cneth to improve the technical management and the safety of thermal muds practices outside of dedicated regulations.

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## BARIUM TRANSFER FROM THERMAL MUDS TOWARD HUMAN BODY : THE T2BT STUDY

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Keywords: mud poultices, barium, blood, urine, spa treatment, transcutaneous passage

#### Introduction

Pelotherapy by poultices is of public health importance in France because 6 million mud-based treatments are delivered annually to around 400,000 spa guests. Curists are treated using heated thermal mud within the context of 9 to 18 consecutive daily sessions of 10 to 15 minutes duration.

Once mixed with natural mineral water, clays represent the main component of the sludge used for thermal baths and a potentially toxic source of barium according to the supervisory authorities. Considering this issue, a study was commissioned by the French Association of Thermal Research (Afreth) to the Institut du Thermalisme, University of Bordeaux, in order to assess the barium concentration in blood and urine samples before and after poultices applications. We chose poultices from clays demonstrating the highest barium content among all the products available in France for hydrotherapy (approximately  $110 \pm 0.1$  mg/kg of barium dry matter).

#### Aims

We aimed to determine the intensity of barium diffusion within the human body from a sample of healthy volunteers, following poultice applications (after 15 sessions over 3 consecutive weeks).

The main objective was to detect a significant increase in plasma barium level i.e a doubling of this level.

Secondary objectives included the detection of barium plasma and whole blood levels exceeding the National Research and Safety Institute (INRS) criteria (1.2  $\mu$ g/L and 7  $\mu$ g /L respectively), the search for a doubling of urine barium levels (normal: 1  $\mu$ g/L) and the evaluation of sludge clinical tolerance.

#### Materials and methods

The mud poultices used for this clinical trial were first swelled (day 0) in sodium chloride natural mineral water. Then they were stored in a poultice oven with a capacity of 25 trays, specifically designed for thermal use. BD Vacutainer® tubes containing lithium heparin and Monovette® tubes were used for blood and urine samples, respectively. Thirty-six volunteers aged between 18 and 30 years were included in this study according to defined inclusion and exclusion criteria and distributed in one of the three 15 day-sessions. On day 1 of each run, the inclusion visit with the investigating physician, a blood and urine samples collection, and finally the application of mud poultices were performed for each participant. The poultice applications were repeated for 15 days and, on day 15, blood and urine samples were collected again before a final medical check-up.

The assay of barium in blood and urine samples was performed using the inductively coupled plasma mass spectrometry (ICP MS) technique (Elan DRCe<sup>TM</sup>, Perkin Elmer) with a precision of around 0.05 per thousand.

#### Results

The full study was done on 35 individuals (30 being the minimal number required with regards to statistical validity).

We demonstrated that there was no significant variation in blood barium levels before and after applications of sludge poultices which remained under the upper limit recommended by the INRS.

The study did not evidence any correlation between blood / urine levels (initial / final) and body mass index, percentage of body fat, or gender.

#### Conclusion

We chose deliberately experimental conditions promoting an optimal diffusion of barium within the body such as participant inclusion criteria (young age, absence of obesity and excess body fat) and the use of a clay rich in barium. Thus, the absence of significant changes in blood and urine barium levels under such extreme conditions allows us to unambiguously conclude that there is no risk of barium overexposure in relation to the application of sludge poultices.

Funding: Cneth, Afreth (Paris, France)

# LEAD, STRONTIUM, ALUMINUM, THORIUM AND MANGANESE TRANSFERS FROM THERMAL MUDS TOWARD HUMAN BODY. FATE OF THESE METALS IN NATURAL MINERAL WATERS AND THERMAL MUDS

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Keywords: mud poultices, blood, urine, spa treatment, transcutaneous passage, mineral water, mud, lead, strontium, aluminum, thorium, manganese

#### Introduction

Pelotherapy by poultices is of public health importance in France because 6 million mud-based treatments are delivered annually to around 400,000 spa guests. Curists are treated using heated thermal mud within the context of 9 to 18 consecutive daily sessions of 10 to 15 minutes duration.

Once mixed with natural mineral water, clays represent the main component of the sludge used for thermal baths and a potentially toxic source of metal elements.

#### Aims

Considering the absence of significant barium diffusion from thermal mud poultices to human organism (cf T2BT study, abstract n°xxxxx) we aimed 1/ to look for possible barium exchanges between clay and natural mineral water, 2/ to assess the possible diffusion of other potentially toxic metals (lead (Pb), strontium (Sr), aluminum (Al), thorium (Th) and manganese (Mn)) in human body, by studying the biological specimens (blood, urine) collected during the T2BT protocol.

#### Materials and methods

The mud poultices were first soaked in sodium chloride natural mineral water. Then, they were stored in a poultice oven with a capacity of 25 trays, specifically designed for thermal use. BD Vacutainer® tubes containing lithium heparin and Monovette® tubes were used for blood and urine collection, respectively. Thirty-six volunteers aged between 18 and 30 years were included in this study according to defined inclusion and exclusion criteria and distributed in one of the three 15 day-sessions. On day 1 of each run, the inclusion visit with the investigating physician, blood and urine samples collection, and finally the application of poultices were performed for each participant. Poultice applications were repeated for 15 days and, on day 15, blood and urine samples were collected again before a final medical check-up.

Natural mineral water and clay samples were treated beforehand by centrifugation and a semi-quantitative multi-elemental screening was then carried out on each of the supernatants by induced plasma mass spectrometry (ICP-MS) (Elan DRCe, Perkin Elmer) using the TotalQuant® mode.

Sr, Pb and Th assays were performed by ICP-MS (Elan DRCe ™, Perkin Elmer) and that of Al and Mn by induced plasma atomic emission spectrometry (ICP-AES) (ICAP 6300 DV ™, Thermo Scientific).

#### Results

The migration pattern of metals studied (Pb, Sr, Al, Th and Mn) between natural mineral water and clay is specific to each element and should be the subject of further study. The study was done on 35 individuals (30 being the minimal number required with regards to statistical validity).

This study on 35 subjects (30 being the minimal number required with regards to statistical validity) demonstrates that there is no significant variation in blood and urine levels of Pb, Sr, Al, Th and Mn before and after poultice applications (p > 0.05). Anyway, these levels remain under toxicity thresholds determined by the National Research and Safety Institute (INRS).

#### Conclusion

At this stage, no conclusion can be drawn regarding metal elements exchanges between natural mineral water and clay.

On the other hand, applications of clay-based sludge poultices containing potentially unsafe heavy metals are not associated with a significant diffusion of these elements in human organism and, therefore, are devoid of toxicity.

#### THERMAL FLOW OF PELOIDS

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Keywords: Thermal flow; Specific heat; Cooling curve; Heat amount; Peloid

#### Introduction

Peloids enable the application of heat to very specific zones and to release heat at a given rate. The rate of heat flow is the amount of heat that is transferred per unit of time, usually measured in joules per second. The aims of this work are to study 16 reference peloids used in medical spa.

#### Materials and methods

Sixteen peloids used in the medical spas (MS) from Europe, America and Israel have been used.

The centesimal composition was quantified by desiccation at 105°C and expressed as a percentage relative to the whole peloid. Water content was calculated by the difference with respect to the percentage of solids. Ash is the residue of the solid components left

behind after incineration at 850°C, expressed as a percentage relative to the whole peloid. The lower the ratio of the % of ash to the % of solids, the lower the materials' content of substances that are volatile or removable by high temperatures. Knowing the centesimal composition makes it possible to deduce the type of solid phase that constitutes the peloid, inorganic or organic.

For the calculation of the Specific heat (Cp), we used the equation proposed by Armijo et al. [2016] with which the specific heat of a peloid can be calculated as a function of its ash (A) and water (W) contents. (Cp) is used to calculate the amount of heat (Q) that a peloid can give.

The peloids cooling curves were prepared by plotting temperature against time. The thermometer used measure product temperature at 15 s intervals from 45°C to 36°C. These curves were then used to obtain the relaxation time (tr) defined as the time needed for the temperature to drop exponentially by 37 % of its starting value (1/e = 0.37). Accordingly, for a peloid applied at 45°C and attaining a final temperature of 36°C, in the first tr the temperature reached would be (36+9/e) 39.3°C. Over 3 times its tr, the temperature reached would be 36.4°C.

From (Q) and (tr) the  $\Phi$  (heat flow) is obtained, that is, the speed of the passage of heat

#### Results

The ash: solids ratios of the 16 MS are provided in Table 1. These ratios indicate that the first 4 peloids have peat as their solid phases while the last 10 show the presence of inorganic materials. The peloid from Héviz originates from the peat base of a lake at a depth of 38 metres which could explain its intermediate ash/solids value. The Copahue peloid shows a reduced ash content due to the presence of volatile sulphur compounds given its volcanic origin.

In Table 1, we also provide (Cp) along with the tr and, Q released by 1 kg of peloid as the temperature drops from 45 to 39.3°C (tr temperature), and  $\Phi$  from the start of the application until the tr is reached. The higher tr were recorded for the peloids based on organic material, peat, meaning they release their heat more slowly than those prepared with inorganic solid phases. For distilled water, the tr determined under the same conditions as for the MS was 230 s, much lower.

#### Conclusion

Considering the centesimal composition of these products, it can be concluded that the ash / solids ratio of the peloids used in the medical spas (MS) studied, indicates that a value close to zero corresponds to the organic solid phases, while values close to one correspond to the inorganic phases. All the medical spas (MS) studied, both organic and inorganic, showed a heat flow rate of up to four times lower than that shown by the same amount of water

Table 1.	Centesimal	composition.	specific heat.	relaxation tir	me, heat amoun	t and heat flow

Medical Spa	Ash/Solids	J/kgK	tr (sec)	Heat (J)	$\Phi$ (J/s)
Františkovy Lázně (Czechia)	0.03	3.7	744	14,136	28.3
Polanczyk (Poland)	0.04	3.8	726	21,717	29.9
Caldes de Bohí (Spain)	0.10	3.7	684	21,204	31.0
Bad Bayersoien (Germany)	0.13	3.8	696	21,432	30.8
Copahue (Argentina)	0.36	2.9	648	15,789	25.2
Heviz (Hungary)	0.45	3.5	624	15,789	32.2
Dead Sea (Israel)	0.77	1.9	400	10,831	27.1
Lopagan (Spain)	0.85	2.0	400	11,571	28.9
El Raposo (Spain)	0.88	2.2	468	12,654	27.0
Thalasia (Spain)	0.88	2.9	498	16,644	33.4
Carhue (Argentina)	0.90	2.8	578	15,789	27.3
Peruibe (Brazil)	0.91	2.9	534	16,416	30.7
Archena (Spain)	0.92	3.4	708	19,437	27.5
Terdax (France)	0.93	2.4	456	13,908	30.5
Arnedillo (Spain)	0.94	1.9	324	10,831	33.4
Poços de Caldas (Brazil)	0.95	2.5	564	14,136	25.1

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#### **HEAT HYGIENIZATION OF THERAPEUTIC MUDS**

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Keywords: Thermal hygienization, poultices, thermal mud, heatchamber, SARS-CoV-2

#### Introduction and objectives

In order to face the Covid-19 sanitary crisis in France, preventive measures aiming at the resumption of the thermal spa activity had been set up by the "cellule prévention et gestion de la crise sanitaire Covid-19" of the National Council of Thermal Spa Operators, in the frame of a sanitary referential (validated by the General Direction of Health on May 28, 2020) [1]. In addition, in its press release of June 15, 2020, the French National Academy of Medicine recommended a heat treatment at 70°C for 30 minutes to inactivate SARS-CoV-2 [2].

In order to meet the recommendation of thermal sanitisation of thermal muds, the Institut du Thermalisme (University of Bordeaux) proposed to study the thermal behaviour of several muds substrates, namely: 2 mixtures of clays based on montmorillonite and kaolinite (Argicur® and Assistherm®), a peloid (Terdax®) and a kaolinite (Imerys®). In parallel, the secondary objectives are the study of the thermal process of the poultice heat chambers and a review of the literature on the calorific capacities of mud substrates.

#### Materials

The study was carried out using a poultice heat chamber with a capacity of 25 trays (Capic®) commonly used in thermal spa resorts.

The metrology was carried out with the help of a central temperature unit (Océasoft®) connected to 9 probes distributed over three distinct zones (bottom, middle, top) and in three different environments (air, water, poultice core).

At this stage of the study, only tests on Argicur® poultices (composed of 90 % montmorillonite and 10 % kaolinite) have been carried out.

#### Method

The poultices were first soaked in natural chloride sodium mineral water at room temperature for 4h, before being placed in 25 trays each containing 3 units.

The heat chamber was programmed to perform various thermal sanitization cycles: 60°C for 2h, 70°C for 2h, 80°C for 2h, 80°C for 1h, 80°C for 30 min, and 80°C for 45 min. The least energy-consuming cycle, which achieved the main objective, was triplicated. The detailed data of the thermal sanitization cycles were retrieved by the Océasoft® software.

#### Results and discussions

tests were performed on the Argicur® substrate. The test at 80°C for 1 hour was conclusive with good repeatability. A thermal sanitization of more than 70°C was

achieved for the three core tests of the poultices, with the following means and standard deviations

- 45 ( $\pm$  6.8) minutes in the low zone
- 80 ( $\pm$  6.0) minutes in the middle zone
- 105 ( $\pm$  7) minutes in the high zone.

These results highlight a poor homogeneity of temperatures in the heat chamber, which can be explained by the presence of an opening in the lower part of the enclosure generating significant heat losses.

The cooling phases revealed a high heat capacity of the Argicur® substrate, with the following return times at 50°C

- 421 ( $\pm$  18.9) minutes in the low zone
- 527 ( $\pm$  11.3) minutes in the middle zone
- 510 ( $\pm$  19.1) minutes in the high zone.

#### Conclusion and perspectives

With a cycle programmed at 80°C for 1 hour, SARS-CoV-2 would be inactivated in the Argicur® substrate according to the results obtained. Other tests following the same methodology will be carried out on the other substrates to obtain the corresponding adequate programming.

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## THERMOPHYSICAL STUDY OF A PELOID WITH MINERAL WATER FROM THE LAIAS SPA

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Keywords: thermophysical properties; peloids; mineral water, clay; microalgae

#### Introduction

In this work, a study of the thermophysical properties of mixtures of a bentonite and the

microalgae *Chlorella sp* with the mineral water of the Laias Spa (Ourense, Spain) is presented. The properties studied are density, thermal conductivity, specific heat and thermal diffusivity as a function of the percentage of mineral water, clay and microalgae used.

#### Materials and methods

The water used is from the Laias Spa (Ourense, Spain). The properties of Laias mineral water are described in Maraver et al., 2020.

The clay used belongs to the company Benesa (Bentonitas Especiales S.A.) located in Murcia, Spain. This clay is described in Casas et al., 2011. It has more than 98 % of phyllosilicates, the predominant clay being smectite.

The microalgae is of the genus *Chlorella sp* [Legido et al., 2015]. It was supplied by the company Porto-Muiños S.L. (A Coruña, Spain).

The studied proportions of bentonite and microalgae are between 5 and 15 % by weight. The specific heat has been determined using a Calvet microcalorimeter [Glavas et al., 2017]. The density of the mixtures was carried out using a pycnometric method [Ortiz de Zarate et al., 2010]. A Decagon KD2 Pro conductivitymeter has been used to measure thermal conductivity [Caridad et al., 2014]. Thermal diffusivity was calculated from the data obtained on thermal conductivity, density and specific heat [Casas et al., 2013].

#### Results

The density of the samples increases with increasing bentonite concentration. They have a density between 1000 and 1140 kg/m<sup>-3</sup> which is relatively low, due to the high percentage of water they contain.

Thermal conductivity increases with increasing bentonite and *Chlorella sp* concentration. The values of the thermal conductivity of the studied peloids are between 0.55 and 0.65 W·m<sup>-1</sup>·K<sup>-1</sup>, which can be considered a normal conductivity for this type of systems.

The specific heat decreases with increasing bentonite concentration and varies very little with the concentration of *Chlorella sp*. The specific heat of the studied mixtures varies between 3400 and 4000 J·kg<sup>-1</sup>·K<sup>-1</sup>, being high values, due to the high percentage in water. The thermal diffusivity of the studied samples shows an increase with increasing bentonite concentration and with an irregular behaviour with respect to the concentration of *Chlorella sp*. The values of the thermal diffusivity of these peloids are between  $0.14 \cdot 10^{-7}$  and  $0.16 \cdot 10^{-7}$  m<sup>2</sup>·s<sup>-1</sup>, being the usual values in this type of mixtures.

#### Conclusions

The samples with the highest proportion of mineral water would be suitable for use in bathing tubs. On the other hand, those with a lower content of mineral water would be applied in the form of cataplasms (mud packs). Mixtures of intermediate concentrations would be applied as envelopments (a thin layer of mud followed by wrapping) which have the best possibilities to obtain good results in both therapeutic and cosmetic applications in thermal centres.

#### Acknowledgments

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# Evaluating method for the therapeutic effects of a Techirghiol sapropelic mud extract by hyperspectral imaging and biological investigations (HISMUD Method)

## Constantin Munteanu, Mihaela Antonina Calin, Mihail Hoteteu, Diana Munteanu, Gelu Onose (Romania)

We developed a new, interdisciplinary, combined method, using an association of hyperspectral imaging (HSI) with biological investigations, named HISMUD method, for evaluating the health effects of an innovative natural product represented by an extract from Techirghiol sapropelic mud, which contains humic and fulvic substances, The method (Hismud method) developed and used for evaluating the effects on health of an innovative mud extract, on three interlinked levels:

Molecular and cellular biological investigations: on primary dermal fibroblasts cultures, obtained from Wistar rats, on which the research team will test and investigate the cellular and molecular mechanisms influenced by mud extract. Research at the molecular and cellular level, by electrophoresis, Elisa and Western blotting of two main physiological mechanisms, respectively the inflammatory processes and the oxidative status, will constitute the basic biological level from which we can think to build a scientific scaffolding for the possible therapeutic effects of Techirghiol mud extract.

Systemic biological investigations: on laboratory animals (Wistar rats: healthy animals

and pathological cases of experimentally induced arthrosis) by applying on their skin of our mud extract and in parallel the Techirghiol mud itself. Using hyperspectral imaging (HSI), we can objectify the vascular effects and tissue oxygenation properties of our mud extract comparative with Techirghiol mud applications, used now in the Sanatorium, with unquestionable clinical effects, sustained by more than 120 years of balneary tradition. Blood investigations will be also performed, to relate the inflammatory markers and elements of oxidative status, bringing biological data necessary to interpret the HSI information in a systemical context.

Human studies: on healthy volunteers and arthrosis patients, using a hyperspectral imaging - non-contact, non-ionizing, non-invasive, and label-free method - as a new medical application, can objectify the vascular effects and the tissue oxygenation properties of our mud extract comparative with Techirghiol mud applications, in correlation with biological data related to inflammatory and oxidative state (balance or stress) of the human organism.

Previous scientific data show that, during the inflammatory process, different cell types are recruited, including fibroblasts, which respond to various intercellular and microenvironment signals. This leads to the regulated production of different pro- and anti-inflammatory mediators including cytokines, such as tumour necrosis factor (TNF)-  $\alpha$  and interleukins (IL)-1 $\beta$  and IL-6, chemokines, and inducible enzymes such as cyclooxygenase (COX)-2, all of them play critical roles in controlling the inflammatory process. The concept of oxidative stress caused by toxic free radicals represents the basis of taking into account the biomarkers of oxidative balance. The oxidative and reductive activity of enzymes that act on glutathione, thioredoxin and other substrates of interest in the oxidation-reduction process reflects not only the level of antioxidative protection but are also relevant biomarkers including for rheumatic degenerative diseases.

In a prior study, we made the fractionation of humic substances from Techirghiol sapropelic mud using the pH and solvent polarity variation and was spectrophotometrically characterized based on absorption in the wavelength range 340-700 nm humic acids and fulvic acids differentiated on the basis of solubility and molecular mass. The quality of organic substances in peloids was evaluated by two methods, namely the ratio of humic acids to fulvic acids and the ratio of the absorbances of the alkaline extract to 465 and 665 nm. The ratio of humic and fulvic acids to Techirghiol's sapropelic mud is 37.52 and A450/A670 decreases from 14.53 to 8.50 in the hydroalcoholic extract. These values are comparable to those of fulvic acids for which the A450/A670 ratio is between 6 and 18.5. The absorption spectra in the range of 340-700 nm show the general characteristics observed for humic substances, decreasing with the increase of the wavelength in an exponential form described by a function of type  $a(\lambda) = a(\lambda r)e-Se(\lambda - \lambda r)$ . The alkaline extract spectrum reflects the properties of the pH 1: low insoluble humic acid fraction with a high content of acid and aromatic groups but low content of O and N groups and the remaining fraction in the solution are mainly composed of extremely rich organic material aromatic and aliphatic [1].

HSI imaging has found its utility in a wide array of applications in numerous fields, such as mining and geology, agriculture, surveillance, astronomy, chemistry and environment. This technique is a relatively new optical method for the medical field with large possibilities for application in the detection of cancer, diabetic foot ulcer prognosis, peripheral vascular disease assessment etc.

Hyperspectral images are produced by instruments called hyperspectral imaging systems or imaging spectrometers. These systems are built around three main components; a light source, a spectral separator (prism, grating, or optical bandpass filters, either tunable or fixed), and a detector (such as conventional 2D charge-coupled device). The light source is directed onto the surface of an object. After entering and passing through the object, the light is reflected, transmitted, and/or absorbed. The diffuse reflected light then passes through a spectral separator that spectrally discriminates the reflected light into a large number of spectral bands. Finally, the light reaches the detector, where is collected as a two-dimensional image containing spectral data inherent in each pixel that is transferred to a computer for processing and analysis. HSI combines the possibilities offered by spectroscopic techniques with the advantages of digital imaging. It consists of an acquisition of a series of images in many adjacent narrow spectral bands and reconstruction of the reflectance spectrum for every pixel of the image (1). The set of images thus obtained (typically tens or hundreds of images) is called the hypercube. The image hypercube has three dimensions: two dimensions represent the spatial coordinate of a pixel and one dimension gives the wavelength of a particular spectral band. Thus, both spatial and spectral information about an object or scene under investigation can be obtained at the same time from analysis of the hypercube.

Studies on ten healthy volunteers, applications with Techirghiol mud on the dorsum of the left hand of each volunteer, for 20 min. A push broom hyperspectral imaging system was used to acquire images of the volunteers' hands at different moments of the pelotherapy: 0 min, 5 min and, 20 min and after 20 min post-pelotherapy. Oxyhemoglobin and deoxyhemoglobin distribution maps on the hands of the volunteers at all these moments of pelotherapy were generated from hyperspectral data. Oxygen saturation maps were also generated at the same time moments. The results have revealed that pelotherapy modifies local blood concentration; increased oxyhemoglobin concentration and decreased deoxyhemoglobin concentration. This could bring new insight into the physiological response to pelotherapy and may become a step forward in understanding its mechanism of action. The results have been shown that pelotherapy is effective in improving local blood oxygenation parameters, at least in healthy volunteers. This opens the door for new research in both pelotherapy and hyperspectral imaging, and the results of these researchers would not only interest the medical world but also could extend to applications of hyperspectral imaging from remote sensing into medical fields.

### MUDS RECONDITIONING AFTER USE: THE "ARGICUR BIOSECURE LINE"

#### F. Albrecht, G. Albrecht, Argicur Company (France)

The Argircur company has been created by Guy Albrecht, chemist engineer (ESSTIN, Nancy Polytechnic Institute) and works under strong human values for a better human health and sustainability of therapeutic natural resources.

The company medical work has been continuously based on a clear and scientific know-ledge of the care using thermal muds made of natural mineral water (NMW) and specific clay. So, the company objectives are aimed on thermal muds properties.

This comprehensive approach offered a relevant knowledge of treatments, allowing the understanding and creation of a patented technology (without chemical products adjunctions) to separate clay from the liquid (NMW). Thus, we can offer to various thermal care facilities to treat joint pain with a fully natural product (without any chemical compound), in order to both protect earth resources and reduce rubbish wasting. So, through these different processes, it is possible to upgrade the thermal muds after the patients treatment and to guarantee an optimum care.

This innovative and patented process aims to divide mud (composed of clay and NMW) in solid and liquid phases allowing a restitution of a clay similar to the clay extracted in the quarry. The production line is processed on two pillars: i) an exquisite time and temperature in the industrial oven and ii) a strict micronization. The gain of the process is a 30 % saving of earth resources and 80 % saving of waste disposal.

This industrial process has been worked out with the scientific support of the Compiègne University and can be fully beneficial for every thermal care facility. Moreover, it has been patented by Argicur and Choquenet Company ("Haut de France"). It is possible to visit on demand the bio-resourced line on the production site (under confidentiality rules).

The company is continuing to work-out research with the support of a robust scientific committee in the scope of always more practical applications to improve human health and earth resources sustainability.

# EVOLUTION OF THE HEALTH SAFETY FRAMEWORK FOR MUD AND UPDATE OF THE GOOD PRACTICES GUIDE FOR BALNEOTHERAPY CENTRES

Terry, W., Fouquey, J.P., Ainouche, R., Bouvier, C.E., & Robin, C. Aquacert International – 3 rue du golf, parc Innolin – 33700 Mérignac w.terry@aquacert-international.com

Key words: mud / health safety / Good Practices Guide

Aquacert International is a French association whose purpose is to lead multistakeholder committees and to publish standards of good practices and certification for the water sector. Aquacert international has published numerous papers and standards for balneotherapy sector and for the water sector more generally.

#### Introduction

Following a referral from the French National Academy of Medicine (ANM) to confirm the presence and impact of barium in mud, the National Union of balneotherapy centres (Cneth) has decided to conduct a multi-stakeholder committee and associated workgroups aimed at improving overall knowledge and health safety methods for muds. Aquacert International has been mandated by Cneth to lead this committee.

#### Method

A steering committee bringing together representatives of the most significant stakeholders has been set up. Chaired by a representative of Cneth and led by Aquacert International, this steering committee defined thematic working groups and thereafter invited French experts to work together.

- \* GT1: Quality management system for mud producers
- \* GT2: Quality management system for balneotherapy centres using mud.
- \* GT3: good practices / analysis standards
- \* GT4: barium and heavy metalsResults

This presentation is about the results of GT1-GT2 -GT3 only. The results of GT4 will be presents by another speaker)

This 10-month working process resulted in a strong mobilization of the balneotherapy professionals (more than 50 participants in total). The clay and mud suppliers were particularly involved, and the discussions were carried out productively. Many decisions have been validated, with the aim of improving health safety.

These improvements decided by the workgroups and validated by the Steering committee have induced a major update of the Good Practices Guide about the following aspects.

- Health safety and HACCP requirements for the suppliers
- Analysis methods
- · Health vigilance

#### Conclusion

It was a necessary deepening of the subject of muds and a useful update of the requirements for the surveillance and heath safety system for mud cares. This approach has led to a major update of the Good Practices Guide which seizes this opportunity to become a fully web and mobile permanent edition of the Good Practices Guide for balneotherapy centres.

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## MUD-BATH THERAPY – BIOLOGICAL MECHANISMS OF ACTION

Antonella Fioravanti<sup>1</sup>, S. Cheleschi<sup>1</sup>, E. Ortega Rincón<sup>2</sup> - Lecture

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Keywords: Balneotherapy; mineral waters; mud-bath therapy; rheumatic diseases; mechanism of action

#### Introduction

Balneotherapy (BT) comprises a broad spectrum of therapeutic modalities including hydrotherapy, bath in mineral water, mud-pack therapy or the use of edaphic remedies usually practiced in health resorts. Recently, BT has been widely used as non-pharmacological approach for the treatment of different rheumatic diseases, including Osteoarthritis (OA), Fibromyalgia Syndrome (FS), Low-back pain and Spondiloarthritis, for its beneficial effect on pain, function, quality of life and its favorable economic profile.

The mechanisms by which immersion in mineral or thermal water or the application of mud alleviates suffering in rheumatic diseases are not fully understood, and the therapeutic activity of BT is probably the results of a combination of mechanical, thermal and chemical effects.

Non specific or hydrotherapic mechanisms are due to the physical properties of the water

and are related to the simple baths in hot tap water. Otherwise, specific or hydromineral effects depend on the organic and inorganic compounds as well as on the community of microorganisms present in mineral water, in mud or in other peloids with therapeutic properties.

The purpose of this paper was to examine the highest evidence provided by a number of clinical and preclinical studies aimed at investigating the possible mechanism of action of BT in rheumatic diseases.

#### Methods

A research from the literature about the studies investigating the beneficial effects of BT in rheumatic disorders has been performed examining the period from January 2011 to December 2020. A search in scientific databases Pubmed, Scopus and Embase was performed. The keywords selected for the research were "spa therapy", "balneotherapy", "mud-bath therapy" in combination with "rheumatic diseases". Studies were considered eligible if were totally written in English language, and classified as original articles whose main objectives were to analyze the effects of BT.

#### Results

The results of clinical studies confirmed the beneficial properties and the positive effects of BT in limiting the production of the main pro-inflammatory cytokines, prostaglandins, heat shock proteins, and adipokines in patients with OA. The ability of BT in regulating oxidant/antioxidant balance was observed in patients suffering from RA, FS, and OA. Furthermore, the main markers of bone and cartilage damage and metabolism, and a pattern of miRNA were positively modulated by BT in patients with OA, osteoporosis, and affected by chronic degenerative musculoskeletal disorders.

The data derived from OA and RA-induced murine models revealed the efficacy of different BT treatments in decreasing pain, inflammation and improving mobility, as well as in reducing the expression of matrix degrading enzymes and markers of oxidative stress.

Different in vitro studies analyzed the potential effect of mineral elements of mineral waters, especially H<sub>2</sub>S, demonstrating their anti-inflammatory, antioxidant and chondroprotective properties in fibroblast-like synoviocytes and chondrocytes, and in macrophage monocytes. The ability of H<sub>2</sub>S donors to reduce oxidative stress and regulate bone metabolism was confirmed in human and rat primary or transformed cell lines of osteoblasts and osteoclasts, and in human mesenchymal stromal cells derived from bone tissue.

#### **Conclusions**

In the last decade, evidence derived both from clinical and pre-clinical studies corroborated the anti-inflammatory, antioxidant, chondroprotective, and immunosuppressive role of different mineral waters or mud applications, confirming the role of BT as complementary therapy for the treatment of various rheumatic diseases.

However, more research should be conducted to further evaluate the long-term efficacy of BT, and a higher methodological quality of treatment modalities needs to be determined in future studies. A general improvement of pre-clinical studies is imperative to limit the high heterogeneity and to allow a standardization of the experimental procedures. Again, the analysis of the only inorganic composition of thermal waters is not enough, but it is also necessary to consider their organic fraction that may play a role in the therapeutic efficacy or in other biological mechanisms. Finally, the question concerning the absorption of mineral elements into the skin and subsequently their concentration into the circulation remains unsolved. All these adjustments could contribute to increase the knowledge about the biological mechanisms underlying the beneficial effects of BT.

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# HISTOLOGIC AND IMUNOHISTOCHEMICAL STUDY ON ASPECT OF DERMIS AFTER BALNEOTHERAPY WITH SAPROPELIC MUD FROM TECHIRGHIOL LAKE, ROMANIA

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Keywords: mud therapy, dermis, neoangiogenesis, immune cells

#### Introduction

Nowadays classic histology and classic balneology, both seems to be obsolete. Optical microscope and bathing in mineral waters in medical purpose both are out of date for research. The normal histological aspect of different tissues has already been described many tens of years ago and balneotherapy appears more a luxury than evidence based medicine, an application that acts on the function without changing the structure. The aim of the study is to evaluate if mud therapy produces modification within dermis that can be highlighted by histological and imunohistochemical techniques.

#### Materials and methodes

#### Materials

- Sapropelic mud and mineral water from Techirghiol lake,
- Glycerinate extract of medicinal plants,
- Biopsy from deltoidian region meaning subcutaneous and muscle proofs, (1,5/0,5 cm),
- Laboratory reactive, fixators, solvents, specific dyestuffs, microtom, research microscope, equipped with automatic expometer and video camera, soft of image analysis Lucia© G.

#### Methods

- 30 patients who received mud-therapy (wrapping, bath, ointement) and 5 who received non-peloid bath, during 12 days,
- Including and exclusion criteria were applied upon the four batches,
- Biopsy collection have been made from the deltoid region, at the end of balneal cure. The cropping have been made at the Emergency Unit from Constanta University Emergency Clinical Hospital, in the surgery room, respecting all the requirements of a small surgical intervention/biopsy. Fragments having dimension 1,5/0,5/0,5 cm have been recorded, numbered and processed in classical histological technique fixation in

formol, inclusion in paraffin, sectioning paraffin blocs, gluing on the blade and staining with routine stain and muscle specific stain, then examined with a Nikon E–600 microscope and acquired with a Sony video camera . The images have been processed using the Lucia $\[ \]$  G soft of image analysis and analysed statistically. The patients were clinically evaluated and biological investigated before starting the treatment.

#### Results

Superficial dermis-1. increase of the blood vessels caliber. 2.vessels of neoangiogenesis. 3.perivascular inflammatory infiltrate with: lymphocytes, plasmocytes and Rouget cells. Deep dermis: 1. slight vascular congestion; 2. perivascular lymphocyte infiltrate with positive reaction at CD45 and negative reaction at CD20.

#### Conclusions

Balneal cure with sapropelic mud of Techirghiol produces highlighted histological and imunihistochemical changes: neoangiogenesis vessels, the increase of the caliber of the blood vessels, the presence of the perivascular inflammatory infiltrate, absence of B lymphocyte, presence of plasmocyte and Rouget cells and presence of T lymphocytes.

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# HISTOLOGICAL AND BIOHISTOMETRICAL SIMPLE STUDY ON EPIDERMIS MELANIN DEPOSITS AFTER BALNEOTHERAPY WITH SAPROPELIC MUD FROM TECHIRGHIOL LAKE. ROMANIA

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Keywords: mud therapy, epidermis, melanin, melanocyte, keratinocyte

#### Introduction

Nowadays, balneotherapy appears more a luxury than evidence based medicine, an application that acts on the function without changing the structure. The study aims to evaluate melanin deposits within keratinocytes and melanocytes after mud application,

through histological methods.

#### Materials and methods

#### Materials

- sapropelic mud, mineral water from Techirghiol Lake, glycerinate extract of medicinal plants and all the facilities for bathing from Balneal and Rehabilitation Sanatorium Techirghiol, Romania,
- skin biopsy of 1,5/0,5 cm from deltoid region and facilities of Emergency Unit from Constanta University Emergency Clinical Hospital;
- blood samples for cortisol and thyroid stimulating hormone determination,
- laboratory reactive, fixators, solvents, specific dyestuffs, microtome, research microscope equipped with automatic expometer and video camera, soft of image analysis Lucia© G of Ovidius University, Faculty of Medicine, Histology discipline.

#### Methods

- 30 patients who received mud-therapy (wrapping, bath, ointment) and 5 who received non-peloid bath, during 10 days of treatment/12 days of staying,
- Including and exclusion criteria were applied upon the four batches,
- blood samples for determining serum level of hormones (cortisol and thyroidstimulating hormone) have been cropped before the beginning of cure, at 24 hours after first application and at the end of the cure,
- The histological proofs have been collected at the end of cure, processed by conventional histological method and have been analysed at photonic microscope,
- Through biohistometry were evaluated the charge with melanin of the epidemical cells determining the report between the area occupied with melanin and the total epidemic area.

#### Results and discussions

Analysis of blades shows statistically significant increase of melanin in the basal and deep spinous layer and in melanocytes at all three types of mud administration.

The most intense melanin presence was detected at the lot that made the ointment with cold mud (expected result), where the melanin is disposed in all the keratinocytes' cytoplasm followed by the patients from the plot who received mud pack (unexpected results); the quantity of melanin within the skin cells of the patients who received plant extract bath was not statistically significant;

Hormones variation evaluation shows decrease of serum level of cortisol, statistically significant for mud wrapping, increase of serum level of thyroid-stimulating hormone, statistically significant for mud wrapping and for cold mud ointment.

#### Conclusion

The increasing amount of melanin pigment in the keratinocytes' and melanocytes' cytoplasm, presented on histological blades and confirmed by biohistometry and statistical analysis is a morphological proof of histologic modification induced by peloid therapy through the neuro-endocrine mechanisms. Increasing melanin presence within

cells is correlated with decreasing serum level of cortisol: the highest charge melanin and the lowest cortisol serum level were at the batch with cold mud ointment, the second place, very close by first, is occupied by mud wrapping and the third place belong to mud bath

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## MUD THERAPY: THE ACTUAL MEDICAL BENEFIT AND DATA OF EVIDENCE

#### Tamas Bender (Hungary) - Lecture

Mud therapy has been used alone, as well as along with balneotherapy for several years to treat patients suffering from locomotor diseases. A recent overview of medical databases conducted has provided insight into the prognosis of mud therapies alone and in combination with balneotherapy in already published articles that confirm significant improvements in their usages overall for treatment of Osteoarthritis (OA), although, as for inflammatory rheumatic disease the evidence was less.

As part of that ongoing research, Randomised Controlled Trials were found, including double blind studies, that were issued, which strengthen the hypothesis that the efficacy of mud therapies do decrease pain to improve the quality of life. Besides this, some data are available the using of mud in skin and gynecological diseases. The method of application were: alone mud therapy, combined with spa water or mud bath therapy.

On the base of recent evidence mud therapy itself or in frame of other complex physiotherapy is a very useful treatment for the rheumatic patients.

### THE EFFECT OF MUD BATH AND MUD WRAP ON THE BLOOD PRESSURE

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#### Introduction

Previous studies show that mud therapy has a normalizing effect on cardiovascular functions [Ekmekcioglu et al., 2000; McAlindon et al., 2014; Merati et al., 2014; Costantino et al., 2015]. The aim of the current study was to measure the effect of mud bath or mud application on blood pressure.

#### Methods

An experimental study was performed in three Estonian spas: AS Värska Sanatorium, Heal AS, and Tervis Medical Spa. Participants were divided into two groups: mud bath with mineral water, 40–42 °C and mud wrap, 40–42 °C. No control groups. Treatments were done in the morning at least two hours after breakfast and last for 15 minutes. Every participant had only one mud procedure. The electrocardiography was taken, and a health questionnaire filled before the treatments. The blood pressure and pulse rate were measured before and after the treatment and also after 60 minutes. Previously prescribed medications were taken as usual. In the study associations of blood pressure, heart rate, signs of left ventricular congestion and/or hypertrophy in the electrocardiogram, body mass index (BMI), and hypertension risk factors with cardiovascular reaction during the mud therapy were evaluated.

#### Results

An experimental study was performed with 133 persons in two groups: 72 of them had a mud bath and 61 mud wrap. The groups had similar age, biometric data, and hypertension risk factors. The mud bath group participants had more males, higher blood pressure values before treatment, and used less medications.

There were individual differences in both groups, but mean changes showed a decrease in blood pressure values: in the mud bath group from 145/90 mmHg to 135/85 mmHg after the bath and after 60 min no changes. Mud bath lowered the mean blood pressure 3–9 mmHg. Mud wrap did not change the mean blood pressure and stayed at 135 mmHg. Heart rate rose after both procedures and normalized after one hour back to the initial value. The maximum value was recorded at 125 beats per minute. Left ventricular hypertrophy was correlated with higher blood pressure before and after the treatments. Blood pressure medications did not influence the blood pressure value during the treatment. Unwanted reaction to higher blood pressure was detected more in smokers, participants who reported higher emotional stress level, and diabetics.

#### Conclusion

Mud therapy does not elevate the mean blood pressure in hypertonic subgroups. The mud bath and mud wrap treatment had quite similar effect on cardiovascular function. Mud therapy has the effect to normalize the blood pressure – initial higher values were normalized after the treatment and normal values did not change significantly after mud therapy. Heart rate among participants was slightly higher directly after the treatment but normalized after one hour.

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## PELOIDOTHERAPY IN RHEUMATOID ARTHRITIS, A PILOT RANDOMIZED CLINICAL TRIAL

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Key words: Peloidotherapy; Rheumatoid arthritis; Balneotherapy; Pain; Quality of life

#### Aim

To compare short and middle term (up to 3 months) effects of peloidotherapy + usual care with usual care alone on pain, function and quality of life in patients with rheumatoid arthritis (RA).

#### Methods

RA patients were recruited in the Medical Ecology and Hydroclimatology department of Istanbul Medical Faculty and were randomized into two parallel groups. Peloidotherapy group was treated with heated mudpack (41-42°C) on painful and active joints (5 days/week, during 2 weeks) + usual care. Control group received usual care alone. Randomization was performed by using a computer-generated table of random numbers and was blinded. The sequence was concealed until interventions were assigned. The

investigator was blinded. The assessments were done before and after the intervention, 1-month and 3 months after the completion of treatment. The main criterion was the number of patients with low disease activity (DAS  $28 \le 3.2$ ) at the end of follow-up. Other judgment criteria were pain (VAS), patient's global assessment (VAS), physician's global assessment (VAS), Health Assessment Questionnaire (HAQ), Disease Activity Score (DAS 28), CRP & ESR.

#### Results

56 patients were recruited and analysed: 29 in peloidotherapy group and 27 in the control group between 11/2011 - 02/2012. At the third month, 9/29 patients were in low activity in peloidotherapy group and 4/27 in the control group (p=0.15). There was a statistically significant improvement in favour of peloidotherapy group for HAQ during all follow-up period ( $0.25 \ vs \ 0.63, p$ =0.007 at the end of the treatment,  $0.29 \ vs \ 0.68 \ p$ =0.007 at the  $1^{st}$  month and  $0.30 \ vs \ 0.59, p$ =0.040 at the  $3^{rd}$  month). Pain ( $35 \ vs \ 50, p$ =0.028), patient's global assessment ( $37 \ vs \ 53, p$ =0.028), physician's global assessment ( $33 \ vs \ 48, p$ =0.030), and DAS28 ( $3.76 \ vs \ 4.58, p$ =0.049) improved significantly more in peloidotherapy group at the  $3^{rd}$  month. There were no between group differences for ESR and CRP. There were no important adverse events.

#### Conclusion

Even though there is no statistical between-group difference for the main criteria, most of the other judgment criteria improved more in the peloidotherapy group than in the control group. A trial with a higher statistical power is necessary to confirm the short and middle term efficiency of this treatment modality on pain and quality of life.

#### PELOTHERAPY RESEARCH IN IBEROAMERICA

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Keywords: Peloid; Mud therapy; Iberoamerica

#### Introduction

The aim of this presentation is to show the situation of research on Pelotherapy research in Iberoamerica.

#### Materials and methods

The search was conducted on first March 2021, in the following databases: Medline (via PubMed) and Web of Science (2017-2021; Clinical trials and reviews; English language) carried out in Iberoamerica countries.

#### Results

28 relevant papers found. Paper subjects: Thermal therapy (8/28.6 %); Peloid properties (13/46.4 %); Solid and liquid phases (5/17.9 %) and Organic materials (2/7.1 %).

Article type: Originals (19/67,9 %) and Reviews (9/32,1 %).

Year publication: 2017 (6/21.4 %); 2018 (7/25 %); 2019 (5/17.8 %); 2020 (7/25 %) and 2021 (3/10.7 %).

Origin: 5 countries; Spain: (20/71.4 %); Cuba (3/10.7 %); Portugal (3/10.7 %); Argentina (1/3.6 %) and Brazil (1/3.6 %).

#### Conclusion

Pelotherapy research in Iberoamerica is active. The most of publications are in journals with good impact factor and better ranking

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#### **BIOLOGY**

#### BACTERICIDAL EFFECT OF HOT SPRING WATER FROM KAWAYU ONSEN

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Keywords: bactericidal effect; acidic hot spring water; Kawayu Onsen

#### Introduction

There is a legend that athlete's foot improves when you soak in hot spring water at Kawayu Onsen. Furthermore, Escherichia coli is rarely detected where Kawayu hot spring water is flowing into the river. On the other hand, it has been reported that the bactericidal effect of Staphylococcus aureus etc. was observed in Kusatsu hot spring water with pH 2.1 [Inoue et al.,1999]. Because the pH of Kawayu hot spring water is 1.73, which is more acidic than Kusatsu hot spring water, it is considered that it has the same bactericidal action.

#### Methods

After obtaining informed consent, 19 subjects soaked one arm in hot spring water and the other in tap water at the same time to the depth of the wrist for 5 minutes at around 36°C. During the immersion, they were seated in chairs and had their hands shake in the water about once every 30 seconds. After pulling out the hands from the water, they waved their hands to drain the water, and let them air dry for 1 minute. Then the entire palm was pressed against the palm shaped culture medium and the medium was immediately covered. The medium was sent to the laboratory center and the number of colonies that had grown was counted to examine the bactericidal effect of hot spring water.

#### Results

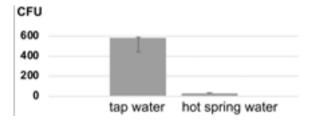


Figure 1. Colony forming units (CFU) after soaking in tap water or hot spring water (n=19). p<0,0005 (Wilcoxon signed rank test, mean - or + SEM)

#### Conclusion

Colony forming units were significantly lower after soaking in hot spring water than in tap water, which suggested that hot spring water from Kawayu Onsen has bactericidal effects. Recently, hot spring water from Kusatsu Onsen reported to have the effect of inactivating the Covid-19 virus (not published data). Hot spring water from Kawayu Onsen might also have the same power against Covid-19 virus.

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### BENEFICIAL EFFECTS OF NATURAL MINERAL WATERS ON INTESTINAL INFLAMMATION AND THE MUCOSA-ASSOCIATED MICROBIOTA

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**Purpose**: Natural mineral water (NMW) intake has been traditionally used in the treatment of various gastrointestinal diseases, such as gastric dyspepsia and irritable bowel syndrome. We investigated the effect of two French NMW, one a calcium and magnesium sulphate, sodium chloride, carbonic and ferruginous water (NMW1), the other a mainly bicarbonate water (NMW2) on the prevention of intestinal inflammation.

**Methods**: Two natural mineral waters (NMW) were used in the present study: NMW1, a sulphate-carbonic-ferruginous water from thermal springs of Châtel-Guyon, France; and NMW2, mainly a bicarbonate water from thermal springs in Vichy, France. Intestinal epithelial cells were stimulated with heat inactivated pathobiont Escherichia coli or H<sub>2</sub>O<sub>2</sub> exposure to induce a pro-inflammatory response, and NMW was added to evaluate the anti-inflammatory effects. In a mouse model, moderate or severe colitis was induced by 1 % and 4 % dextran sulfate sodium (DSS), respectively, in Balbc/J mice drinking NMW1 or NWW2 or control water. General signs of colitis, fecal lipocalin-2 levels, pro-inflammatory KC cytokine release in colon samples, histological features of colitis and the mucosa-associated microbiota were analyzed.

**Results**: Using intestinal cells in culture, we demonstrated that both NMW1 and NMW2 exhibited anti-inflammatory effects. In mice with moderate induced colitis, NMW1 was effective in dampening intestinal inflammation, with significant reductions in DAI scores, fecal lipocalin-2 levels, pro-inflammatory KC cytokine release and intestinal epithelial lesion sizes. Moreover, NMW1 was sufficient to prevent alterations in the mucosa-associated microbiota. In terms of phyla, treatment with NMW1 and NMW2 led to a higher proportion of Firmicutes and lower percentages of Bacteroidetes and

Proteobacteria, a sign of the establishment of a less colitogenic microbiota. Statistical analysis of differences in the microbiota composition between mice treated or not with NMW1 thermal water using LEfSe analysis demonstrated that NMW1 led to significant increases in Candidatus arthromitus (segmented filamentous bacteria, SFB) known to promote Th17 cell differentiation and lactic acid bacteria of the Lactobacillus type. A 3-week treatment with these NMW is sufficient to significantly shift the mucosa-associated microbiota composition toward a more balanced and less colitogenic microbiota.

Conclusion: To conclude, this study showed that both tested NMW from Châtel-Guyon (NMW1) and Vichy (NMW2) exhibited anti-inflammatory properties in in vitro and in vivo models more important with NMW1. These anti-inflammatory effects could be mediated by rebalancing the mucosa-associated microbiota composition, which is usually destabilized during inflammation. However, our work also showed that this treatment is less effective in severe colitis models, suggesting less relevance for the management of active disease. Thus, spa treatment could be discussed to maintain a state of low inflammation rather than to treat active diseases needing more effective pharmacological treatments. The use of spa treatment as a complementary therapy to extend periods of "low grade" inflammation in IBD patients would be investigated by relevant clinical investigation, assessing the impact of spa treatment on the composition of the intestinal microbiota and determining the relations between patients' improvement and rebalancing the intestinal microbiota.

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### GASES ABSORPTION THROUGH THE GASTROINTESTINAL TRACT. AN APPROXIMATION

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Keywords: Hydroponic cure; Gastrointestinal absorption; Thermal gases intake

#### Introduction

Nutrients are absorbed by highly polarized intestinal epithelial cells and usually enter the bloodstream. Different mechanisms, active and passive, govern this phenomenon throughout the entire intestinal length.

Dissolved gases in some mineral-medicinal waters have the peculiarity of incorporate in the lumen content, being there modified or not, by its physicochemical characteristics and being passively absorbed into blood flow. Lumen osmotic concentration, pH, electrical signals and other phenomenon has an essential influence.

#### Method

Numerous studies have focused on the implication of gases in the treatment of disease. It should also be considered that dissolved active stomach gases are pH-dependent [Carbajo & Maraver, 2017; Litou et al., 2020]. In general, the most active forms originate at acidic pH, as gases, in the stomach (pH between 1.0-3.0), and are modulated after neutralization into duodenum by the massive release of bicarbonate [Takeuchi et al., 2011]. There is a transformation of the dissolved gases into their soluble salts. This phenomenon occurs in the small intestine and colon (pH between 6.0-7.5 and 5.5-7.0 respectively) and can be modified over the years [Merchant et al. 2016].

#### Results

Hydrogen sulfide (H<sub>2</sub>S) can be ingested through sulfurized mineral-medicinal waters and can also originate in the gastrointestinal system itself by the intestinal microbiota (H<sub>2</sub>S-producing colonic bacteria) [Blachier et al., 2019; Blachier et al., 2020], mainly by oxidation of intestinal sulphates [Khushkevych et al., 2020], where it is an agent of stability at the microbiome-mucosa interface [Wallace et al., 2018].

H<sub>2</sub>S has been shown have anti-inflammatory and antioxidant effects dose-dependent and can regulate the blood flow of the gastric mucosa. After an alteration of the gastric mucosa, the stomach H<sub>2</sub>S concentration decreases, probably due to acidification and its consequent oral release. It has also been confirmed that in addition to H<sub>2</sub>S, CO and NO play an important role in the mucosal defence mechanism and gastroprotection [Han et al., 2017].

It is well documented that the gut microbiome can affect the host's immune system in many ways, both in health and in disease [Illiano et al., 2020]. The concentration of H<sub>2</sub>S in the colon and its generation or inhibition is decisive for the immune system [Dilek et al., 2020]. Consequently, the local bacterial load and the acidification/alkalization of the medium are of vital importance in gases or salts formation of the same species [Shen et al., 2013].

Finally, it has been shown that administration of H<sub>2</sub>S (sulphurous waters) can protect and repair the damaged gastric mucosa [Shen et al., 2019].

Carbon dioxide gas (CO<sub>2</sub>) is part of the CO<sub>2</sub>/carbonate system and carbonic anhydrases enzymes are those that, together with lumen pH, regulate its reversible transformation into carbonic acid, bicarbonates and carbonates, the main mechanism of the regulation of cellular and physiological pH [Occhipinti, 2019]. Consequently, its responsible of microbiota regulation, of pH physiological maintenance and gastrointestinal barrier function [Lee & Hong, 2020], although in the colon short-chain fatty acids are metabolized to CO<sub>2</sub> and ketone bodies [Macfarlane & Macfarlane, 2012]. The special characteristics of the CO<sub>2</sub>/bicarbonate system with pKa = 6.35 make it decisive for the stabilization of the intestinal mucosa and microbiota regulation.

#### Conclusion

The gases contained in sulfurous and carbonated mineral-medicinal waters have a

notable influence on intestinal function and can modify intestinal physiology, allowing design possible therapeutic strategies for the treatment of disorders related to regulation of pH and intestinal microbiota.

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## SALTS ABSORPTION THROUGH THE GASTROINTESTINAL TRACT. AN APPROXIMATION

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Keywords: Hydroponic cure; Gastrointestinal absorption; Thermal gases intake

#### Introduction

Electrolyte transport takes place in the intestinal epithelium, both in the small intestine and mainly in the colon [Helander & Fandriks, 2014], that has a structural organization that allows processing of 9 L of liquids and excreting only 100 mL. Intestinal electrolyte transport is a balance of ion secretion and absorption processes through active and passive mechanisms, where water quality is very important [Presta et al., 2021].

#### Method

Main transporters involved in intestinal secretion are Cl- channels, Na<sup>+</sup>-K<sup>+</sup>-2Cl- cotransporter (NKCC2) and NKCC1 and K<sup>+</sup> channels. Absorption mainly involve Na<sup>+</sup>/H<sup>+</sup> (NHE) and Cl<sup>-</sup>/HCO3<sup>-</sup> exchangers in the small intestine and proximal colon and Na<sup>+</sup> channels in distal colon [Rao, 2019]. Likewise, the proportion of salts in gastrointestinal lumen can originate cellular osmotic processes, even other mechanism, that affect intestinal transit or viability of physiological and microbiome cells [Carbajo & Maraver, 2018].

Absorption of cations has several mechanisms. Some of them such as Na<sup>+</sup>, employ different absorption mechanisms in small intestine (nutrient transporters and NHE) and colon (electroneutral NaCl transport and Epithelial sodium channels-ENaC) [Kiela & Ghishan, 2016; Bigiani, 2020].

Calcium and Magnesium are absorbed in jejunum and ileum. Ca<sup>2+</sup> has a different mechanism based on diet, depending on having a rich diet (diffusive paracellular pathway) or poor (vitamin D and Transient Receptor Potential cation channel-TRPV6). This is not Mg<sup>2+</sup> case,

which is absorbed by passive and active transport through TRPV6 and TRPV7 and Divalent Metal Transporter 1 (DMT1) [Blaine et al., 2015]. The importance of maintaining magnesium intake for our body has recently been valued [Fiorentini et al., 2021].

Other minerals, such as iron and copper, have to be previously reduced. Fe<sup>3+</sup> is absorbed in duodenal brush border, being reduced to Fe<sup>2+</sup> by cytochrome-B reductase-1 (DCYTB; CYBRD1), before being absorbed with dietary ascorbic acid or DMT1 [Fuqua et al., 2012]. Otherwise, Cu<sup>2+</sup>, mainly in the stomach and duodenum, is transformed into Cu<sup>+</sup> by cytochrome B reductase 1 (CYPBR1) and its absorbed by apical high-affinity copper transporter 1 (CTR1; SLC31A1) and DMT1 [Doguer et al., 2018].

Cations trace elements have a varied absorption capacity. Bivalents (Zn, Mn, Cd) are usually absorbed through DMT1 in duodenum and proximal jejunum, although they may also have specific mechanisms [Kiela & Ghishan, 2016]. Selenium absorption appears to be carried out by amino acid transporters Solute Carrier Family 3 Member 1 (SLC3A1 and SLC1A4) and it appears to be a saturable process in the enterocyte [Fairweather-Tait et al., 2011; Ha et al.; 2019].

Cl<sup>-</sup> ion is absorbed through three different mechanisms: paracellular (passive) pathway in the small intestine; in ileum and colon by exchange of Na<sup>+</sup>/H<sup>+</sup> and Cl<sup>-</sup>/HCO<sub>3</sub><sup>-</sup> mainly NHE3; and HCO<sub>3</sub><sup>-</sup> dependent Cl<sup>-</sup> absorption to stabilize intestinal lumen pH [Rao, 2019]. SO<sub>4</sub><sup>2-</sup> ion is transported in intestine through two mechanisms: transport mediated SLC13A1 (Solute Carrier Family 13 Member 1, Na<sup>+</sup>-dependent), insensitive to pH, and by transport mediated by SLC26A1 and SLC26A2 which also acts on the exchange of sulfate/oxalate, sulfate/bicarbonate or oxalate/bicarbonate [Markovich, 2012].

#### Results

It is important to note that absorption of minerals and trace elements should be studied as a whole. Indeed, intestinal absorption of calcium and magnesium not only depends on the concentration of these minerals, the presence or absence of phosphates, pH of the medium (pKa) and other circumstances significantly vary their absorption performance and even their properties.

In a similar way it happens with the companion ion of the element, absorption of sodium through NaCl (pka = 3.09) is not parallel to NaHCO<sub>3</sub> (pka = 10.33 to carbonate and pka = 6.35 to carbonic acid), where independently of salt, pKa has its remarkable importance.

In this sense, influence of microbiota quality is decisive [Cresci & Bawden, 2015]. The presence of acidophilic or fermenting microorganisms can greatly condition the intestinal absorption of molecules. Conversely, mineral-medicinal waters can influence too on quality of microbiota.

#### Conclusion

A clinical understanding of the transport of nutrients through the gastrointestinal tract allows us to understand the mechanisms of action of the different mineral-medicinal waters and obtain better clinical results.

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# A COMPREHENSIVE ANALYSIS TO UNDERSTAND THE IMPORTANCE OF IN VITRO RESEARCH TO STUDY THE MECHANISM OF ACTION OF BALNEOTHERAPY: WHY, HOW, AND WHERE IT CAN BE USED?

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Keywords: Balneotherapy; Mineral waters; in vitro studies; Cell cultures

Balneotherapy (BT) is a complementary therapy that generally employs mineral and/or thermal waters from natural springs, peloids (mud), and other traditional remedies, and represents one of the most commonly used complementary therapies for many pathological conditions, including rheumatic and skin diseases. The beneficial effects of BT are principally related to physical and chemical factors, but the exact mechanism of action is not fully understood. Recently, there has been an increased interest in the use of preclinical models to investigate the influence of BT on inflammation, immunity, and cartilage and bone metabolism.

The objective of this comprehensive analysis was to analyze the current knowledge about the potential role of in vitro research to study the mechanism of action of BT in different pathological conditions. The analysis was focused on underlying the advantages or drawbacks related to their use to study the biological effects of mineral waters, as well as their limitations.

Our analysis showed that in vitro studies take the advantage to represent simplified, rapid and inexpensive biological systems, useful to improve the knowledge about the potential mechanism of action of mineral water, tested as a whole or as singular mineral element or as organic fraction, at the molecular level.

The choice of the suitable cell culture represents an important and essential key point to obtain the best experimental performance in terms of biological response. Thus, the identification of the most suitable cell model for a specific pathological state, together with the maintenance of the optimal culture conditions, is essential to obtain the best results

However, the usefulness of the culture models is limited by several sources of bias. First of all, their relevance needs to be considered with caution, since the changes that occur in the cells do not necessarily reflect in vivo conditions. Second, their validity is conditioned by a correct experimental procedure, which should take into account the particular and complex composition of mineral waters. Finally, to assess the potential beneficial and/or toxic effects of thermal mineral waters or chemical or organic components the procedures of purification and filtration should be performed, even of it could remove the natural spring water microbiome, recently considered to be responsible for some positive effects of BT in different diseases.

This review corroborate the scientific value of in vitro studies underlining the importance of this approach to understand the specific effect of a mineral water or a

particular inorganic or organic component, in terms of mechanisms of action. However, the validity of the cell culture model is limited by several sources of bias, as the differences in experimental procedures, the high heterogeneity, and the difficulties in considering all the chemical and physical factors of BT. Taken together, all these considerations could represent a rationale to stimulate the scientific community to standardize the experimental procedures and enhance in vitro research in the field of BT.

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# AN UPDATED ANALYSIS ABOUT THE MECHANISM OF ACTION OF BALNEOTHERAPY IN RHEUMATIC DISEASES: RESULTS FROM IN VITRO STUDIES

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Keywords: Balneotherapy; Mineral waters; Hydrogen sulfide; Cell cultures; Rheumatic diseases

#### Introduction

Balneotherapy (BT) is a complementary therapy that generally employs mineral and/or thermal waters from natural springs, peloids (mud), and other traditional remedies, and represents one of the most commonly used complementary therapies for many pathological conditions, including rheumatic diseases. The beneficial effects of BT are principally related to physical and chemical factors, but the exact mechanism of action is not fully elucidated. Recently, there has been an increased interest in the use of preclinical models to investigate the influence of BT on inflammation, immunity, and cartilage and bone metabolism.

The objective of this comprehensive analysis was to summarize the current knowledge about the in vitro studies in BT and to revise the obtained results on the biological effects of mineral waters. Special attention has been paid to the main rheumatologic diseases.

#### Methods

A research from the literature about the in vitro studies investigating the biological effects of BT in disease conditions has been performed examining the period from January 2000 to December 2020. The strategy used to select pre-clinical researches consisted in a search in scientific databases Pubmed, Scopus and Embase. The keywords selected for the research were "spa therapy", "balneotherapy", "mud-bath therapy" in combination with "rheumatic diseases", "cell cultures", "in vitro studies", "chondrocytes cultures", "synoviocytes cultures", and "fibroblasts cultures". Studies were considered eligible if were published from 2000 to the present, totally written in English language, and classified as original articles whose main objectives were to analyze the effects of BT.

#### Results

The properties of a thermal water, tested as a whole, or of its inorganic components, such as hydrogen sulfide (H<sub>2</sub>S), were analyzed in different cell cultures. The results of the studies demonstrated that H<sub>2</sub>S donors (NaHS and GYY4137) induced anti-inflammatory, antioxidant and chondroprotective properties in arthritic fibroblast-like synoviocytes and chondrocytes. The ability of H<sub>2</sub>S donors to limit the oxidative stress damage was also confirmed in human primary or transformed cell lines of osteoblasts and osteoclasts. Finally, the anti-inflammatory and chondroprotective activities of a strongly acidic sulfate mineral water was observed in human OA chondrocytes, and the regulation of osteogenic differentiation and bone mineralization was found in human mesenchymal stromal cells derived from bone tissue treated with sulfurous thermal waters.

#### **Conclusions**

Collected results corroborated the scientific value of in vitro studies in demonstrating the anti-inflammatory, antioxidant, and chondroprotective role of BT, at the cellular level, in rheumatic diseases. This approach allows to understand the specific effect of a mineral water or a particular inorganic or organic component, in terms of mechanisms of action. However, the validity of the cell culture model is limited by several sources of bias, as the differences in experimental procedures, the high heterogeneity among the available researches, and the difficulties in considering all the chemical and physical factors of BT. Taken together, all these considerations could represent a rationale to stimulate the scientific community to standardize the experimental procedures and enhance in vitro research in the field of BT.

- 1. Cozzi et al. Balneotherapy in chronic inflammatory rheumatic diseases-a narrative review. *Int J Biometeorol.* 2018;62:2065-71. doi: 10.1007/s00484-018-1618-z.
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### ANTI-OXIDATIVE EFFECTS OF WEAKLYALKALINE REDUCED WATERIN RAW 264.7 MURINE MACROPHAGECELL LINE

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Keywords: Weakly alkaline reduced water; RAW 264.7 murine macrophage cell; anti-oxidative; LPS; H<sub>2</sub>O<sub>2</sub>

#### Introduction

It is well known that oxidative stress and inflammation are closely related with the cause and process of various diseases. In recent years, studies on functional water are developing at a rapid pace, especially on weakly alkaline reduced water(ARW) which contains abundant molecular hydrogen and other essential properties such as alkaline pH and negative oxidation reduction potential. To date, there is no study to show antioxidant effects of weakly ARW on murine macrophage cell lines. Here, we investigated the anti-oxidative effects of weakly ARW at two different pH (8.5 and 10) in RAW 264.7 murine macrophage.

#### Methods

We treated  $H_2O_2$  (0.4mM for 2 hr) and LPS (10 µg/mL for 24 hr), respectively in RAW 264.7 cell line to induce oxidative stress. Cells were then treated with weakly ARW at pH 8.5 and 10 at different concentrations (0.1, 1 and 10 %) for 24 hr. Cell viability, and oxidative stress markers such as reactive oxygen species (ROS), nitric oxide (NO), intracellular calcium and antioxidant enzyme activities were measured.

#### Results

First, our results showed the decreased cell viability upon  $H_2O_2$  and LPS induction, which was significantly rescued upon treatment of weakly ARW in both pH 8.5 and 10.Similarly, the increased ROS, NO and intracellular calcium level caused by  $H_2O_2$  and LPS induction was significantly decreased upon weakly ARW treatment. Moreover, the ARW treatment in  $H_2O_2$  and LPS-induced cells also significantly mediated antioxidant enzymes such as catalase and glutathione peroxidase.

#### Conclusion

Taken together, weakly ARW of both pH, 8.5 and 10, showed the anti-oxidative effects on oxidative stress-induced murine macrophage cells via inhibition of oxidative stress markers and enhancing the antioxidant enzyme activities. Further studies are ongoing to confirm the mechanism of its antioxidant effects.

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#### NATURAL MINERAL WATER

#### THERMO-MINERAL WATER RESOURCES IN ALGERIA

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Algerian thermo-mineral resources have been the subject of several studies since the end of the 19th century to date. The last assessment made it possible to update and deepen our knowledge of their states and evolutions. They went from 90 springs [Bertheraud, 1970] to 282 springs [Bet Beregh, 2015]. We found the different facies: sulphate; sulfide; chlorine; bicarbonate. Temperature was variable from hypothermal to hyperthermal temperatures and, in all the cases, flow rates sufficient for their operation.

To this end, apart from the exploited sources, around a hundred have been prioritized to allow investments in the thermal field for the private sector.

These springs will be protected (protection perimeter and others) investors will be supported in their efforts. These natural resources will be dedicated to health (medical spas) as well to well-being and patients' recovery (rehabilitation).

#### **ALGERIAN SPA RESORTS - THE PRESENT SITUATION**

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For a heritage of 282 thermal mineral springs, less than a hundred are exploited throughout the national territory.

The 8 medicalized thermal spas, as well as a thalassotherapy center (rehabilitation in the marine environment) are approved by the various social security funds. They take care of some pathologies relating to hydrotherapy as well as functional rehabilitation, mainly musculoskeletal conditions and neurological disorders.

Thermo-leisure, well-being and health recovery are supported by both private and public thermal care facilities.

A recent merger with the Algerian university will make it possible to take charge of metabolic disorders (obesity and diabetes) and cardiovascular rehabilitation with programs established in collaboration with specialized hospital cardiologic units.

### POSSIBILITIES OF REVITALIZING THE RENOWNED WATERS OF GALICIA (SPAIN) IN TIMES OF A GLOBAL PANDEMIC

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#### Introduction

The importance that balneotherapy and the treatments provided in spas has on people's health has already been well established. As there is an inexhaustible bibliography that exists for the subject, we'd like to highlight some recent scientific references for the reader: Covillo et. al, 2018: 174, Fernández Torán, et. al. [2018:297], Armijo Castro et. al [2017:91-99], Morer et. al. [2017:249-256], Ferreira Pego [2016:4-18], Aguilera et. al. [2015:61-62], Maraver Eyzaguirre [2015:2297-2312], Saz Peiró [1987,2011:66-70,2019:5-7], Piau Ch. et al. [2020]. The effectiveness of balneotherapy in strengthening the body so as to avoid contracting an infection is mentioned (among the many existing studies) by Galvez et. al 2017 and 2018 a and b. From the most general to the most specific, and which is already adapted to the current scenario, the study by Masiero (2020) is worth highlighting above other studies as he notes that, in this situation marked by Covid-19, it is essential to study and spread awareness surrounding the benefits of balneotherapy for the immune system (based on the fact that mineral waters offer very beneficial effects for one's health).

#### Methods

In line with the importance of hydrotherapy treatments administered in spas for the recovery of Covid-19 patients, as well as from a purely preventive perspective, several inactive (or practically inactive) spas were identified in the Autonomous Community of Galicia. To identify them, help was sought from the guide of mineral-medicinal waters of Galicia, one published by Ramirez Ortega et. al [2007:49-64] and one by Ramirez Ortega et. al [2000:249-265]. Through these guides (and with the support of other works from different origins - medical hydrology, anthropology, landscape geography, etc.) and based on the field work carried out, the various inactive Galician spas under study were located, to look to the possibilities of revitalisation. In accordance with the qualitative methodology, inherent to the field of Human Sciences, the analysis was also based on ethnographic field work and, as always, the locals played an active role in supporting the study as key informants (such as "historical bathers or spa-goers" in these famous waters). The Anthropology-related method was extremely important for us, since the sources and spas chosen for the analysis have been used locally by the surrounding neighbourhood, going beyond their formal use. In addition, they have remained alive and active for a long time by the locals using them (they have not fallen into disrepair and disuse).

Once the inactive spas were located, various spas that remained unused for a long time were focused on and are now in the process being revitalised. The spa that was chosen

specifically to carry out the field was the Spa of Requeixo (Balneario de Requeixo).

#### Results

Following the on-site analysis carried out in several famous spas in Galicia, the information is available in the form of extensive photographic material taken on-location in the spa in which the field work was based, supported by ethnographic work. The results obtained following the analysis from the Landscape Geography of all the natural resources surrounding the famous waters of Galicia are combined with the aforementioned analysis, which complement the spa healing treatments.

#### Conclusion

In this study, four Galician spas (one per province) were analysed but while they were disused, they had more than a merely feasible possibility for revitalisation. They spas have, in fact, springs with great healing and potential health benefits and their waters have been declared waters of public utility. Both the characteristics of the water and the possibility for revitalisation have been reviewed in the field work and have been collected together in this present study. Revitalising the spas seems to be, as previously alluded to, technically simple (it is something common to the four selected spaces). In this current health crisis, which has severely affected the elderly population, it would be possible to bring life back to these spaces - the Imserso Social Hydrotherapy Programme is just one of a number of possible ways- thus benefiting public health, not just the health of senior citizens but also that of the general population. Furthermore, these spaces also tick all the necessary boxes for this new situation (open air, absence of crowds, social distancing) and these have always been present, in one way or another, in the collective thinking.

# NATURAL ENVIRONMENT IMPACT ON PHYSICAL AND MENTAL HEALTH OF WORKING-AGE POPULATION

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Keywords: natural environment, balneotherapy, physical and mental health

#### Introduction

Daily stress affects both physical as well as psycho-emotional health of every person and is argued to cause a number of diseases [Slavich, 2016]. In many cases, these are not only diseases that affect mental health of a person, but also diseases of cardio-circulatory system, digestive tract, and endocrine system. Stress accelerates the development of

inflammatory processes in the body [Yaribeygi et al., 2017]. It is not uncommon for a patient to have more than one illness, which directly worsens their mental health as well. A never-ending cycle is formed – physical health affects person's mental health and vice versa [Euesden et al., 2017]. It is not possible to break such chain and achieve full individual wellbeing with only pharmaceutical treatment, therefore balneotherapy and peloid therapy are increasingly included in the treatment process, also climatic factors that have positive impact on the treatment of various diseases are taken into account [Woźniak-Holecka, et al., 2017].

#### Methods

The literature search was conducted in January of 2020 using "PubMed" and "Google scholar" database search engines. Articles which present research on the effect of natural factors on health and not older than 10 years were analyzed. 44 scientific articles which present data on the positive effect of natural factors on physical and mental health of humans were found and analyzed.

#### Results

Being outside in a natural environment together with physical activity statistically significantly improves both physical and psycho-emotional health of a person [Barton et al., 2017]. The incidence of cardiovascular disease in people living in areas surrounded by greenery is 37 % lower than in those living in urbanised areas [Aerts et al., 2018]. Mineral water procedures reduce the amount of stress hormone cortisol in the body, also helps to maintain a constant balance of neurotransmitter serotonin, which leads to smaller mood and emotional changes when under stress. Balneotherapy reduces excitation of sympathetic nervous system, reduces concentration of oxyhemoglobin in the right side of the prefrontal cortex, which determines the ability to calm down. This improves mental health of a person [Jo et al, 2019]. Chronic pain, as well as depression and psychological fatigue caused thereby are reduced, especially in the intervention group which was able to bathe in thermal waters [Huber et al., 2019]. The application of natural factors in rehabilitation improves and accelerates recovery processes, helps people of the working age to return to the workplace faster [Grahn et al., 2017]. During balneotherapy, biologically active organic and inorganic minerals absorb through the skin and reach certain points of the body, at the same time reducing the number of inflammatory mediators (TNF-α, IL-1β, IL-6) at that point, in patients with rheumatoid arthritis [Gálvez, 2018]. Muscle as well as joint pain is reduced, subjects' quality of life is improved, compared to pre-treatment period [Blain et al., 2016].

#### Conclusion

- 1. Daily presence in nature positively affects personal mental health, reduces the tendency towards depression.
- 2. Mineral water procedures positively affect physical as well as mental health, reduce pain, improve patients' mood and quality of life.

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## ADVANTAGES OF A CLIMATOTHERAPY SITE WITH A FOREST ENVIRONMENT

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Keywords: mood status; net effective temperature; skin temperature; forest; terrain cure

#### Introduction

Japanese people had traditionally used natural capital for their good health. About 70 years ago, there were over 700 sanatoriums in Japan [1]. Climatotherapy is conducted at seaside, forest, uplands and mountain areas, with exposed during several weeks to the suitable biometeorological conditions [2]. Considering the human circaseptan rhythm and to obtain the apparent therapy effect, it is evidently preferable to stay at the health resorts 3-4 weeks [3]. However, today's people can seldom take enough time for rest and relaxation. Based on the German climatotherapy method, we had originated the short version climatotherapy programme to fit anyone who aims for disease prevention and health promotion. This programme was launched in 2014 at Fukui prefecture, in the northwest part of the main island of Japan [4].

#### **Material and Methods**

Our study was carried out at Yatsusugi Forest in the moderate mountain and Fukui Prefectural General Green Center (GC) in a tree-rich lowland park. Yatsusugi Forest has several uphill and downhill paths. The protocol of the programme is shown in Figure 1. Participants was instructed to maintain their subjective temperature under 'slightly cool' conditions to meet the climatotherapy purpose. POMS (Profile of Mood Status) brief form Japanese Edition is composed of six subscales: Tension-Anxiety (TA), Depression-Dejection (D), Anger-Hostility (AH), Vigor (V), Fatigue (F) and Confusion (C). A standardized score by gender and age group (T score) was used because of age disparities among the participants. As peripheral surface temperature, skin temperature of back of the hand was measured with an infrared thermometer. Meteorological data (temperature, humidity and wind velocity) were obtained at on-sites and JMA (Japan Meteorological Agency) Fukui observatory. Net effective temperature (NET) was calculated by Gregorczuk's modification formula [5]. Paired t-test was used for paired groups, and two-tailed p value of less than 0.05 was considered significant. The statistical analyses were conducted using IBM-SPSS ver. 22.0. Our study received ethical approval from The Research Ethics Committee of University of Fukui (No. 20140051).

Climatic terrain cure (2.5 km) and following fresh-air rest cure (20 minutes) were carried out in every session.

The interval between each session was at least one week.

Participants took part in all sessions from the first to the sixth.

	Spring		Autumn			
Yatsusugi Forest (1st session)	GC (2 <sup>nd</sup> session)	Yatsusugi Forest (3 <sup>rd</sup> session)	Yatsusugi Forest (4th session)	GC (5 <sup>th</sup> session)	Yatsusugi Forest (6 <sup>th</sup> session)	

**Figure 1**. Protocol of the short version climatotherapy programme

#### Results

In 2015-2017, 43 urban dwellers (20 males and 23 females) participated in our programme. Mean age was 65.7 (66.9 in men and 64.7 in women). At both sites, mood status TA, D, AH, F and C were improved significantly after climatotherapy session. Only mood status V was not changed significantly, except the 3rd session in which mood status V was improved.

**Table 1**. Paired t-test results (*p*-value) comparing T scores between before and after climatotherapy session.

Sess	sion Site	TA	D	AH	V	F	C
$1^{\mathrm{st}}$	Yatsusugi	< 0.001	< 0.001	< 0.001	0.175	0.013	< 0.001
$2^{nd}$	GC	< 0.001	< 0.001	< 0.001	0.805	< 0.001	0.001
$3^{\rm rd}$	Yatsusugi	< 0.001	0.001	< 0.001	0.001	0.001	< 0.001
$4^{\text{th}}$	Yatsusugi	< 0.001	< 0.001	< 0.001	0.510	< 0.001	< 0.001
$5^{\scriptscriptstyle th}$	GC	< 0.001	0.001	< 0.001	0.900	0.001	< 0.001
$6^{\text{th}}$	Yatsusugi	< 0.001	< 0.001	< 0.001	0.984	0.003	0.001

At both sites, skin temperature significantly decreased during climatic terrain cure (data were not shown).

**Table 2**. Meteorological factors comparison.

(mean)	JMA Fukui (mean)	<i>p</i> -value
gi 18.9	21.8	< 0.001
21.8	21.5	0.089
ıgi 68.3	53.5	< 0.001
57.1	52.6	< 0.001
gi 0.6	3.4	< 0.001
0.7	3.7	< 0.001
gi 16.9	15.6	0.001
18.5	14.6	< 0.001
	21.8 agi 68.3 57.1 agi 0.6 0.7 agi 16.9	gi 18.9 21.8 21.8 21.5 agi 68.3 53.5 57.1 52.6 agi 0.6 3.4 0.7 3.7 agi 16.9 15.6

JMA Fukui observatory is located in the city center. At both sites, humidity is significantly higher and wind velocity is significantly lower than JMA Fukui observatory.

#### Conclusion

In the spring and the autumn, both Yatsusugi Forest and GC site are less sultry and a gentle breeze environment. Even in the lowland climate area GC, mood status was improved and cool body surface was achieved during this programme. These are considered to be significant contributions from the forest environment. The differences between the two sites lie in the altitude and topography, and their effects on the heart rate in relation to the training effect have been described in previous studies [4]. If, for reasons of illness or infirmity, relaxation and rest are the main objectives of climatotherapy, then forest parks may be an option to consider.

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#### THERMAL TOURISM EXPERIENCES AND SELF-RATED QUALITY OF LIFE

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Keywords: thermalism; quality of life; barriers; motivation; life satisfaction

#### Introduction

It is assumed in our society that tourism contributes to improving our mental and physical health in leisure time and thus becomes a precursor to increasing the quality of life. There is evidence in different studies that experiences related to tourism lead to positive psychological and physical states, improving the sense of well-being, happiness, quality of life and satisfaction with life in general. According to those studies, it was found that activities related to tourism have significant influence on well-being, quality of life and above all, it brings satisfaction to the lives of tourists [Woo et al., 2015; Balderas-Cejudo et al., 2017; Hwang et al., 2020].

Within the scope of tourist advantages for the quality of life of the elderly, McCabe and Johnson [2013], Toepoel [2013] and Morgan et al. [2015] consider tourism experiences

to be great enhancers of propensity to promote social interactions and social connectivity. Also, Mélon et al. [2018], as well as Ferrer et al. [2016] and Gu et al. [2016] had already concluded that, compared to non-tourist seniors, senior tourists felt younger, more educated, richer, more involved in physical and social activities in their daily lives, more satisfied with their social relations, and reported higher levels of health than non-tourist seniors.

Nowadays, thermal tourism is widespread throughout the world, due to its millenary therapeutic virtues which integrate classical thermalism and its wellness component. Furthermore, it also embraces relaxation, prevention, leisure and care programs connecting body and mind. The thermal resorts of northern Portugal and Galicia (Spain) are prepared to receive visitors who wish treatments understood in the context of classical thermalism., and also wish to broaden this possibility, by enjoying other leisure-oriented, relaxing and local aspects. This is the increasing trend that has considerably grown and thickened the numbers of users of the thermal baths.

To the best of our knowledge, there are not studies about the perception of the quality of life of elderly tourists attending thermalism. Therefore, the research aims to relate the concepts of tourism, thermalism and quality of life, analyzing the quality of life perceived by elderly thermal tourists in the Northern region of Portugal and Galicia (Spain).

#### Methods

The research methodology consisted of conducting surveys in order to evaluate the quality of life perceived by thermal tourists, from Galicia and northern Portugal, when using the programs offered by thermalism both in its traditional aspect and in its well-being feature. For doing so, we used quality of life domains presented by Kelley-Gillespie [2009], and the motivations and limitations or barriers that influence the quality of life of older tourists determined in the study developed by Woo et al. [2014]. A total of 424 questionnaires were applied to thermal goers, 177 in Portugal and 247 in Spain.

#### Results

The characteristics of the thermalists are: average age 66.9 years, approximately two thirds are women, most with basic studies and 90 % traveled accompanied. The most used treatments were rheumatic and musculoskeletal, then wellness treatments.

With regard to travel barriers, we found that they do not affect the quality of life of the thermalists, which leads us to believe that they use the facilitators and negotiating strategies presented by Huber et al. [2018]. On the other hand, travel motivations were shown to influence overall life satisfaction. Finally, we confirm that the quality of life of the thermalists influences their overall satisfaction with life, as proposed by Woo et al. [2014].

#### Conclusion

In view of the results, we can conclude that thermal tourists have experienced improvements in quality of life and have obtained higher levels of overall satisfaction in their lives.

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#### KITE: KIDS INTERVENTION THERAPY - AQUATIC ENVIRONMENT

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Keywords: Hydrotherapy; Physiotherapy; Early Intervention; Day Care Centers; International Classification of Functioning, Disability and Health (ICF)

#### Introduction

The biopsychosocial (BPS) model, from the perspective of the International Classification of Functioning (ICF), considers the neuropsychomotor development (NPMD) as complex and multifactorial [Araujo; Mélo; Israel, 2018]; by doing so, it agrees with the present-day theories regarding child development. In this perspective, the contexts where the child and their family are inserted, and the demands for neuromotor stimulation can benefit from aquatic interventions, which are excellent tools for this purpose [Araujo et al., 2018], because they associate enriched environments with the family's active participation [Rosenbaum, 2011], with repercussions on the child's NPMD [García et al., 2016].

Despite the heated swimming pool being increasingly used for early intervention in pediatrics, there are gaps concerning the systematization of procedures based on the dimensions of the ICF's BPS model. It is a consensus that research should produce

evidence, but increasing the methodological quality of this therapeutic approach. Therefore, the goal of this paper is to describe the ICF-based Kids Intervention Therapy - Aquatic Environment (KITE), intended for 4- to 18-month old babies who are typical, at risk and/or delayed in neuropsychomotor development (NPMD).

#### Methods

The research was approved by the Research Ethics Committee of the Federal University of Parana (UFPR) and filed at the Brazilian Registry of Clinical Trials (RBR). The KITE, as it is named, is an early intervention program with aquatic activities to be performed with babies 4 to 18 months old who attend day care centers.

The assessments and interventions are systematized according to ICF's BPS model. For the main outcome in the NPMD, the Alberta Infant Motor Scale (AIMS) and the Denver Developmental Screening Test II (DDST-II) were used, and, as secondary outcome in the stimulation received, the quality of life and the aquatic skills, respectively, the Affordances in the Home Environment for Motor Development - Infant Scale (AHEMD-IS), the Pediatric Quality of Life Inventory (PedsQLTM) and the Aquatic Functional Assessment Scale – Baby (AFAS Baby) were used.

#### Results

The KITE is an early intervention program in the aquatic environment, centered on the family and the day care environment, performed twice a week, for 8 weeks, in sessions lasting 45 to 60 minutes. The activities are directed by a physiotherapist with the parent's/guardian's active participation in the pool in the process of stimulating their children. The therapies are performed in small groups, and the activities are carried out in a ludic manner, with children's songs and plays appropriate for their age group, considering the ICF's domain of Activities and Participation.

The KITE is performed in a pool heated to 32°C, following Israel and Pardo's [2000] five phases adapted to the babies: (1) accommodation: going in and out of the pool, experiencing the physical properties of the water, warming up and moving around; (2) familiarization with the liquid environment: rotation, straightening and balance stimuli; (3) relaxation: return to quietness; (4) specialized therapeutic exercises: NPMD milestones stimuli; (5) global organic conditioning: active and free moving.

The activities were developed according to specific functional goals and motor behaviors in three main axes: locomotor, stabilizer and manipulative. All the activities approached the combined use of language stimulation through child songs. Throughout the four weeks of the KITE, the activities followed weekly progression criteria, as the execution of the exercises grew difficult according to the physical properties of the water, considering the condition of the baby's participation. The parents/guardians received a weekly folder with stimulation tips to be carried out at home, as the family is taken into account in the process of interventions, following ICF's BPS model.

#### Conclusion

This study described and systematized an early intervention program in the aquatic environment, called KITE, for the baby's NPMD, systematized and based on ICF's BPS view.

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### RHEUMATOID ARTHRITIS AND WATER EXERCISES – SPA THERAPEUTIC PROTOCOL

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Keywords: Rheumatoid arthritis; Water Exercise; Training; Education; Spa Protocol

Being Patient or Health professional is very different.

That's why education of patient and care giver (complementary believes and knowledges) are vital.

The aim of this presentation is to emphasize the importance of qualitative therapeutic exercise education in water, and before starting balneology treatment, highlighting:

- awarding of precautions and contraindications;
- some gold rules and key words for efficacy and efficiency of exercises;
- refreshing alarm signals and what to do for each one.

Finally I describe the exercises protocol itself (three weeks of a Psycho-Motor program)

- Postural correction
- Mobilisation, Stretching (Range-of-Motion)
- Strengthening (Endurance)
- Aerobic Cardio-Vascular exercises (Endurance)
- Relaxation

I think that it does really matter which kind of therapeutic education for patients and health professionals must be considered for training.

#### RESILIENCE OF MINERAL WATER RESOURCES TO CHANGING CLIMATE

Clément Roques, R. Abhervé, A. Gauvain, G. Chrétien, P. Steer, J-R. de Dreuzy, E. Chatton, L. Longuevergne, O. Bour, M. Klepikova, T. Le Borgne, L. Aquilina - Lecture Université Rennes 1, Cnrs, Géosciences Rennes, UMR 6118, 35000 Rennes, France Email: roquesclem@gmail.com

In the course of the water cycle, part of the rainwater percolates underground and transits for a few tens to hundreds of millions of years before returning to the surface. Groundwater flow conditions and fluid-rock geochemical interactions involved during this journey shape the availability and geochemical traits of mineral water resources. While it is well accepted that climate change and growing exploitations are already affecting water resources both on quantitative and qualitative aspects, the identification of the main processes responsible remains a major scientific challenge.

Climate observations reveal significant changes in precipitation and temperature patterns across Europe. Data show overall increasing temperatures in summer associated with lower precipitation rates, while temperature and precipitation rates are both increasing during winter, especially in the Northern part of Europe. All climate models agree that such intra-year spatio-temporal redistribution of precipitation and temperature anomalies will intensify in the near future, strongly affecting groundwater recharge, flow conditions and residence times. Two main hypotheses can be advanced on the evolution of mineral waters in response to modification of recharge. The first hypothesis assumes that groundwater recharge will overall decrease, implying a partial disconnection with the surface hydrological system with fewer productive springs characterized by higher proportion of deep flows paths. The second hypothesis suggests that greater recharge may occur in some areas. This increase will imply the appearance of shallow flow paths, with increasing connection with surface systems (denser distribution of springs with increasing seepage rates). The impact of such redistribution of flow paths on the geochemical traits of mineral waters is not intuitive. Following the first hypothesis, dissolved solute concentrations may increase at springs where evolution toward longer residence times is expected, while more diluted groundwaters are expected following the second hypothesis. In both cases, the question of deep mineral water discharge remains open. In this presentation, after introducing the main climatic, topographic and geological factors controlling the resilience of mineral water resources from a review of the literature, we will specifically discuss observed trends between climatic and hydrological characteristics of few selected regions characterized by contrasting climate and hydrogeological conditions. We will then provide a glimpse into potential evolution of mineral water resources based on results obtained from hydrogeological simulation forced by IPCC (Intergovernmental Panel on Climate Change) climate scenarios. We will notably discuss to what extent groundwater storage, discharge dynamics and associated residence time distribution may be modified. We will finally conclude the presentation by reviewing technological solutions for the monitoring of mineral water resources in the view to improve model predictability skills. We will specifically present the opportunities offered by fiber-optic based technologies to monitor temperature and groundwater fluxes in wells at high spatial and temporal resolutions. In complement, recent development of in-situ mass spectrometers allows the continuous monitoring of groundwater residence times of mineral waters. Based on fundamental knowledge regarding the functioning of natural systems under changing climate, combined with the opportunities offered by such recent technological breakthroughs, we will discuss strategies for the monitoring and prediction of mineral water resources.

# THE DAX STAINLESS AND C-PVC PILOTS: 2 INNOVATIVE EXPERIMENTAL TOOLS TO MEET HEALTH SAFETY CHALLENGES IN THERMAL CARE FACILITIES

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Keywords: biofilm, materials, prototypes, natural mineral water, tests, water systems

It is essential to preserve the quality of natural mineral water from its origin to the points of use, so as to ensure sanitary safety for patients within the thermal spas. The complexity of water systems may lead to issues linked to microbiological and physicochemical contaminations which are necessary to be solved in order to keep the installations in compliance with the regulations in force.

In order to provide the thermal spa sector with means to achieve this goal, the team at the Institut du Thermalisme - Bordeaux University aimed at finding a relevant solution, i.e. designing and making two original and innovating prototypes which reproduce - in miniature - the natural mineral water system we can find in thermal spas.

These two prototypes are different due to the nature of the materials they are made of. It is possible to get significant improvements in the research: on the one hand, linked to the general working of a thermal water system connected to individual or collective care units and, on the other hand, improvements in the research on keeping the quality of natural mineral water. Also, to solve microbiological and physicochemical contamination issues, chemical and thermal treatments can be used.

# BACTERICIDAL EFFECTS OF A NEW CONCEPT OF HYPOCHLOROUS ACID WATER PRODUCED BY SUBSTANCE-MIXING METHOD AGAINST TYPHOIDAL SALMONELLA

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Keywords: Hypochlorous acid; Mixing method; Salmonella; Biofilm, Poultry, Typhoid

Introduction: Typhoidal Salmonella, the causative agent of fowl typhoid and pullorum disease, is the mainspring of high fatalities in poultry breeds. It can be transferred both horizontally within a flock or penetration through the eggshell, and vertically from generation to generation via trans-ovarian route. In the event of widespread transmission of Salmonella in fowl and poultry, a rational approach would necessitate prioritizing the use of non-antibiotic agents with bactericidal properties. Hypochlorous acid (HOCl) has received massive attention in research as a new concept of disinfectant due to its high sterilizing properties, easy accessibility, and bio-safety. This study was conducted to evaluate the susceptibility of typhoidal Salmonella to HOCl water (Sungjin farm Co. Ltd. Gyeongju-si, Republic of Korea) treatment developed by non-electrolysis and substance-mixing method.

**Methods**: To confirm the bactericidal effect, the groups were divided into 6: NT (Notreatment; Trypticase soy broth), TW (Tap water), 70 % Al (70 % ethanol), L-HOCl [27ppm of available chlorine concentration (ACC)], M-HOCl (51 ppm of ACC) and H-HOCl (106 ppm of ACC) waters. To access effects of typhoidal Salmonella, S. gallinarum and S. pullorum were exposed to these experimental waters.

**Results**: The microbial counts showed that S. gallinarum and S. pullorum were more vulnerable to the treatment of 70 % ethanol and 3 different concentrations of HOCl water compared to TW group. Intriguingly, the 70 % Al and HOCl groups demonstrated biofilm-inhibiting capabilities toward typhoid Salmonella.

**Conclusion**: Collectively, our study indicates that mixing type of HOCl water could be used as a safe and eco-friendly bactericidal for restricting Salmonella biofilms in poultry farms and processing environments.

### BROMINE APPLIED TO DISINFECTION OF SWIMMING POOL WATER. A LITERATURE REVIEW

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  Keywords: bromine, disinfection, by-product, bactericidal activity, toxicity

This paper presents a bibliographical review on the disinfection of swimming pool water with bromine. The formation mechanisms and the mode of action of the disinfectant, hypobromous acid, are discussed. The review of the main bromination by-products (bromamines, trihalomethanes, haloacetic acids, haloacetonitriles, bromate, haloaldehydes, nitrosamines, etc.) shows that some of these by-products are present in pool water at concentrations of a few µg·L-1 to a few tens of µg·L-1. The study for acute and chronic toxicity confirms that these compounds should be monitored (especially dibromoacetic acid and bromate) to ensure the safety of swimmers and technical staff. The biocidal effectiveness of bromine versus chlorine, against pathogenic bacteria present in swimming water, is detailed. It has been shown that the bacterial species Escherichia coli, and Enterococcus faecalis are more sensitive to bromine, unlike Pseudomonas aeruginosa that is resistant to bromine. It has also been reported several cases of irritant contact dermatitis when using bromine though some studies have revealed bromamines to be disinfecting, odourless and non-irritating. Nevertheless, bromine exhibits greater bactericidal activity than chlorine in slightly alkaline and warm water and could replace chlorine in the treatment of atypical swimming pools, although chlorine is less costly than bromine.

# INFLUENCE OF HYDROTHERAPY POOL WATER RECIRCULATION REGIME ON STAPHYLOCOCCUS SPECIES CONCENTRATION AT SUBSURFACE: PRELIMINARY EXPERIMENTAL DATA FROM A PILOT

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Pools are prone to contamination from microbial pathogens from human external microbiota, including mainly Staphylococcus species. These bacteria originate mainly from the skin and rhinopharynx and tend to concentrate at the surface/subsurface. Being protected by films derived from mucus and sebum, they are markedly resistant to biocides.

Our study aimed to evaluate the respective impact of mixed and reverse hydraulicity techniques on the concentration of Staphylococcus species at the subsurface following bathing by four individuals in an experimental pool. Disinfection, filtration and water renewal of the pool were stopped in order to study only the influence of the water recirculation regime.

We found a significant reduction of 31.7 % (Test 1), 50.9 % (Test 2) and 41.9 % (Test 3) in total Staphylococcus species counts at the subsurface when using reverse versus mixed hydraulicity. However, this reduction is not a pollution cut but a pollution shift, resulting from an increase in the outlet water flow rate by overflow channel from 49.3 to 100 %. This experimental model was far removed from real life conditions and associated with a series of limitations. However, it seems that the type of water recirculation regime is a critical factor in the bacterial quality of pool water. These preliminary findings need to be confirmed in additional studies using more realistic conditions.

### HYDROTHERAPY ASSOCIATED INFECTIONS : THE DARK SIDE OF WATER

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#### Introduction

Reducing the risk of infection associated with hydrotherapy is essential, as patients using this therapy may be more susceptible to infection, as well as having a higher risk of contaminating water.

In fact, despite the presence of hygiene and safety protocols across all these centers, the rate of infections remains significant.

Additionally, the prevention of infections associated with thermalism often seems to be neglected and placed in the background.

This review aims to sumarize the published litherature about hydrotherapy associated infections, as well to identify the major pathogenic agents and how to stop them.

#### Methods

We made a litherature review in the follow databases: Medline (via PubMed), ISI Web of Science and Central. We included 9 reviews and clinical cases published in the last 5 years.

#### Results

The main pathogen associated with infections during hydrotherapy programs is Pseudomonas aeruginosa, a well-known agent capable of causing infections in places like the skin in healthy individuals, but which can cause serious complications in more immunocompromised individuals, from burned to polytrauma patients. However, fecal bacteria such as Salmonella, E. Coli or Shigella or viruses such as Adenovirus are considered as other agents that are quite prevalent in these infections.

In 2017, the CDC published and edited the Guidelines for Environmental Infection Control in Hydrotherapy Tanks and Pools, which contain a series of recommendations and procedures that must be followed in order to avoid this harmful effect.

#### Conclusion

Although the existence of health and hygiene protocols is transversal to most hydrotherapy centers, this work intends to demonstrate that the risk of infection is real and that the compliance with the Guidelines published by the CDC must be complied with, as well as the individual education of patients, such as oral and perineal washing, which is often overlooked.

We believe that a more detailed assessment of which microorganisms associated with each type of thermal therapy will be necessary, as well as the review by microbiologists and professionals in the field of thermal systems engineering, capable of finding viable solutions that do not compromise the ability to give response to patients, but decrease the risk of adverse effects to treatment.

#### **SULFIDE WATERS**

### H<sub>2</sub>S INHIBITS HOST PROTEASE TMPRSS2 IN HUMAN AIRWAY CELLS : IMPLICATIONS FOR SARS-COV-2 INFECTION

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Covid-19 pandemic affected now more than 150 million people worldwide, accounting for more than 3 million confirmed deaths. Besides ongoing global vaccination, finding protective and therapeutic strategies is thus an urgent clinical need. SARS-CoV-2 mostly infects the host organism via the respiratory system, requiring ACE2 and TMPRSS2 to enter into target cells. Therefore, these surface proteins are considered a potential druggable target. H<sub>2</sub>S is a gasotransmitter produced by several cell types and is as well part of sulphurous natural spring waters, often inhaled as low-intensity therapy and prevention in different respiratory conditions. H<sub>2</sub>S is a potent biological mediator, with anti-oxidant, anti-inflammatory and, as more recently shown, also anti-viral activities. Here, we tested the in vitro effects of H<sub>2</sub>S-donors on TMPRSS2 and ACE2 expression in human upper and lower airway epithelial cells. We demonstrate that H2S significantly reduces the expression of TMPRSS2 without modifying ACE2 expression both in respiratory cell lines and primary human upper and lower airways epithelial cells. Results suggest that inhalatory exposure of respiratory epithelial cells to natural H<sub>2</sub>S sources may counteract SARS-CoV-2 entry in airway epithelial cells and, consequently, prevent virus spreading into the lower respiratory tract and the lung.

### MOLECULAR MAPPING OF SODIUM SELENITE TARGETS IN NORMAL HUMAN KERATINOCYTES

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The goal of this study was to perform a global mapping of the molecular effects exerted by physiological amounts of selenium on human keratinocytes. To achieve our goal, primary cultures of human keratinocytes were subjected to 24h stimulation with sodium selenite (NaSe) at doses that i) do not impact cell survival and ii) are similar to the concentrations observed in selenium-rich spa waters. Irrespective of the condition tested, we found that more than 2 154 proteins were abundantly expressed by cultured human keratinocytes, as assessed by liquid-chromatography mass spectrometry (LS-MS). These highly expressed proteins comprised one selenoprotein, Thioredoxin reductase 2 (TXNRD2), and its substrate, Thioredoxin (TXN). Using LS-MS, we identified 3 proteins exhibiting statistically significant quantitative changes following NaSe stimulation: the endosomal protein RAB9A9, the RNA helicase DDX42 and, interestingly, the NAD(P) mitochondrial transhydrogenase (NNT also known as nicotinamide nucleotide transhydrogenase). Indeed NNT plays a key role in mitochondrial oxydo-reduction enzymatic reactions in which TXNRD2 is involved. To further map the molecular targets of NaSe in human keratinocytes, RNA-seq analyses were performed on control vs NaSestimulated cultures of human keratinocytes. This approach allowed identifying 12 578 mRNA species with expression levels above the detection threshold in all analyzed samples. From these mRNA species, 11 encoded selenoproteins (among which TXNRD2 and TXN) and 52 were differentially expressed in NaSe-stimulated keratinocytes. Of note, 5 genes coding for selenoproteins exhibited increased mRNA levels under conditions of NaSe stimulation: TXNRD1, TXNRD2, GPX1, GPX3 and SEPW1. Moreover, in the co-expression network linking genes which expression is stimulated by NaSe, TXNRD1 was found to be the main hub gene. However, among the 5 selenoproteins-encoding genes which mRNA levels are increased by NaSe stimulation, only the mitochondrial and cytoplasmic selenoprotein GPX1 exhibited a parallel increase in protein expression, as assessed by western blot. Overall, our results demonstrate that in human keratinocytes, low concentrations of NaSe are able to target several oxydo-reduction enzymatic reactions involving selenoproteins with cytoplasmic and/or mitochondrial localization

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# ANTI-INFLAMMATORY EFFECTS OF THE NOVEL HYDROGEN SULFIDE RELEASING PERSULFIDE D-P\* ON THE CHONDROGENIC CELL LINE ATDC5

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Keywords: H<sub>2</sub>S; persulfides; chondrocytes; inflammation

#### Introduction

Hydrogen sulfide (H<sub>2</sub>S) is an endogenously produced gas exerting a diverse range of pharmacological effects. Besides its antioxidant properties, H<sub>2</sub>S emerged as an important regulator of inflammation. Hence, in this study we examined and compared the effects of the commonly used H<sub>2</sub>S donor sodium hydrogen sulfide (NaHS) with the novel recently described thiol-inducible H<sub>2</sub>S releasing persulfide D-P\* on the chondrogenic cell line ATDC5.

#### Methods

H<sub>2</sub>S release kinetic of persulfide D-P\* was evaluated using a H<sub>2</sub>S electrode calibrated with a NaHS standard curve. ATDC5 cells were pre-incubated for either 1h or 6h with increasing concentrations of NaHS or D-P\* (125-1000 μM) before stimulated with IL-1β (10 ng/ml) and IFNg (100 ng/ml) for 24h. Proliferation of ATDC5 cells was determined using WST-1 reagent. Nitrite and IL-6 levels were quantified by the Griess reaction and Elisa, respectively. Western blot analysis was performed to determine protein expression. Superoxide (SOX) formation was monitored using fluorescence spectroscopy.

#### Results

Data show that H<sub>2</sub>S release of D-P\* was induced by thiols (GSH or L-cysteine). In ATDC5 cells, H<sub>2</sub>S released by either NaHS or D-P\* augmented proliferation in a time and concentration-dependent manner. D-P\* at the highest concentration (1000 μM) decreased nitrite and IL-6 production up to 50 % and 80 %, respectively. The inhibitory effects of NaHS were much less pronounced (15 % for nitrite and 30 % for IL-6). In addition, D-P\* strongly upregulated the stress-responsive enzymes heme oxygenase-1 (HO-1) and NAD(P)H quinone dehydrogenase 1 (NQO1) whereas NaHS had only a small effect. SOX measurement revealed that D-P\* did not induce HO-1 expression by inducing production of SOX or other reactive oxygen species. Furthermore, administration of a CO donor (CORM2) was similar to the effects of D-P\*.

#### Conclusion

In the chondrogenic cell line ATDC5, the slow H2S-releasing compound D-P\* exhibits pronounced anti-inflammatory properties which are superior to the commonly used H<sub>2</sub>S donor NaHS. We propose that the anti-inflammatory effects of D-P\* are dependent on two effects: first to its slow H<sub>2</sub>S release and second through its upregulation of HO-1 and NQO1 and induction of CO production.

Taken together, these data suggest that D-P\* might be considered a promising candidate compound primarily for H<sub>2</sub>S research and secondly for the development of novel therapeutic drugs suitable for treatment of degenerative and inflammatory joint diseases.

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### BALNEOTHERAPY IN SULFUROUS WATER ATTENUATES JOINT PAIN AND PROTECTS AGAINST CARTILAGE DESTRUCTION

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Keywords: Balneotherapy . hydrogen sulfide . osteoarthritis . oxidative damage . cartilage

#### Introduction

Osteoarthritis (OA) is a chronic joint disease that results in progressive cartilage destruction and subsequently joint dysfunction [Kraus VB et al., 2015]. A growing number of evidence indicates that reactive oxygen species (ROS) production is increased in OA causing oxidative stress which may participate in the pathogenesis of this disease. Increased pro-inflammatory responses in the synovium and cartilage contribute to cartilage destruction that in turn amplifies joint inflammation, creating a vicious circle that favors development of joint disorders like OA [Bultink et al. 2012; Robinson et al. 2016]. For instance, inflammatory mediators like cytokines and adipokines could increase the synthesis of matrix metalloproteinases (MMPs), well-characterized enzymes involved in the degradation of the extracellular matrix of the cartilage [Cheleschi et al. 2018; Yang et al. 2017]. Growing evidence indicates beneficial impact of balneological interventions in OA [Antonelli M et al]; however, their mechanisms of

action are still unclear [Burguera E et al., 2014]. Here, we evaluate the effect of balneotherapy in sulfurous water in an OA experimental model.

#### Methods

Experimental OA was induced in Wistar rats by transection of the medial collateral ligament and removal of the medial meniscus of the left knee. Animals were randomized into three groups: non-treated (control) and balneotherapy using sulfurous water (SW) or tap water (TW). Macroscopic evaluation was performed, as well as evaluation of pain levels and analysis of motor function by rotarod test. Histopathological changes in articular cartilage and synovium were also evaluated. The presence of matrix metalloproteinase-13 (MMP-13) and oxidative damage markers was assessed by immunohistochemistry. Balneotherapy was performed by placing the rats in hot water (37°C) SW or TP for 20 min, 5 days per week, from day 7 after surgery to day 40. Animals were euthanized at day 40.

#### Results

Joint destabilization induced joint thickening, loss of joint flexion, and increased levels of pain. At day 40, animals from SW group presented lower pain levels than those from control group. Experimental OA also affected motor function. Balneotherapy in sulfurrich water significantly improved joint mobility in relation to that in tap water. Besides, we observed that cartilage deterioration was lower in SW group than in the other two groups. Likewise, SW group showed reduced levels of MMP-13 in the cartilage. Conversely, we failed to observe any modulation on synovial inflammation. Finally, balneotherapy in sulfurous water diminished the presence of oxidative damage markers.

#### Conclusion

Our results suggest the beneficial effect of balneotherapy in sulfur-rich water on an experimental model of OA, showing a reduced cartilage destruction and oxidative damage. Thus, these findings support the use of balneotherapy as a non-pharmacological treatment in OA.

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### THOUGHTS: GENOMICS AND SULFIDE WATER BATH THROUGH SKIN OF EMOTIONAL RHEUMATOID ARTHRITIS PATIENTS

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Keywords: Genomics; Sulfur Water; Rheumatoid Arthritis; Skin; Emotional Status

Nowadays, the biochemistry research on Rheumatoid Arthritis (RA) and Sulfur Bath have found that many physiological elements modulate several pathways such as neuroendocrine and immunogenic systems. This dynamic process regulates different biological activities related to bio-chemical-physical powers, although they are still not completely understood, especially concerning genomics of groundwater. Furthermore, we have a « functional » immunogenic system, receptor of internal and external signals, and the core of complex interactions between the patient, the RA, the skin and sulfide water. We think it would be interesting to brainstorm about these interactions based on current knowledge...

#### **SCIENTIFIC INVESTIGATION - METHODOLOGY**

### NEW EVALUATION METHODS IN BALNEOLOGY : MAIC AND BAYESIAN TRIALS

**Bruno Falissard - Lecture** 

Université Paris-Saclay, Inserm, Paris, France

Key-words: MAIC, Bayes, Balneology, Evaluation, Evidence based medicine

The recent emergence of targeted therapies in cancerology has been the occasion to change substantially the way medications can be evaluated. In more and more frequent situations, it is no more possible to compare with head-to-head randomized controlled trials all the potential treatments that are available for a given disease.

New statistical methods and designs have been developed to tackle these situations. They could be used with benefits by professionals involved in the evaluation of thermal cures. Among these methods, we will consider:

**Matched Adjusted Indirect Comparison** (MAIC), a new approach of indirect comparisons that take the opportunity that, in most situations, investigators have individual data for at least one trial. These individual data can be used to make indirect comparisons more reliable.

**Bayesian randomized controlled trials** add prior knowledge to the information coming from the patients actually included in the trial. This is particularly relevant when the treatment that is evaluated is already proposed to patients for many years. The benefit of such an approach is that sample sizes are much lower.

#### PATIENT PREFERENCE IN BALNEOTHERAPY CLINICAL RESEARCH

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Keywords: Patient preference; methodology; clinical research; balneotherapy

#### Introduction

Patient representations about balneotherapy are important in clinical research as they induce preferences. Because double blind is more often not possible, patient preferences may have an impact both on external and internal validity. In a previous study evaluating the impact of spa therapy in the treatment of knee osteoarthritis, our team showed that 2,4 % (11/462) of patients refused randomization. Moreover 7,2 % (16/223) and 10,5 % (24/228) of included patients respectively in the control group and in the spa therapy group changed to the other one despite the use of a design built to control preference bias (Zelen design) [1]. Attrition and contamination biases tend to be more frequent when patient preferences exist. And both motivation and compliance may vary [2]. Systematic

reviews showed that effect sizes associated with patient preference were more often limited. Nevertheless, effect sizes superior to 0,5 have also been reported [3–5]. According to Kowalski et al., a patient preference effect could occur when strong differences exist between interventions, when active participation is needed, and when expected outcomes and complications vary between interventions [6]. Our aim was then to describe research designs that account for patient preference, and to discuss those which are the most suitable to investigate balneotherapy.

#### Methods

We conducted a literature review. We searched in Medline and Google scholar databases for articles in english published until 2019. Articles must discuss trial designs related to patient preference in order to get included.

#### Results

Patient preference could be handled in two ways: some designs aim to control preference bias and others allow to measure its effects. Patients in crossover and N-of-1 trials get all interventions but it is necessary to test the presence of residual effects. In a waiting list design the control group get the intervention after measuring the outcome [7]. Two designs, inherited from Zelen, control preference bias by randomizing before the patient gives informed consent [8]. Fully randomised control trials use preference as a covariate in their analysis. The randomization process in partially randomized control trials only apply to no-preference patients. They allow preference effect evaluation with selection bias [9]. Finally, doubly randomised control trials evaluate preference, selection and treatment effects with a significant increase in sample size [10]. By studying pros and cons in the balneotherapy context, we found that crossover and N-of-1 trials were not adapted. Waiting list and Zelen designs were the most appropriate to control preference bias. And doubly randomised control trials were the best option for an evaluation of preference effects.

#### Conclusion

Patient representations and preferences may impact balneotherapy clinical research in many ways. Designs have been proposed to control preference or to measure its effects. By studying pros and cons ine the balneotherapy context we found that waiting list and Zelen designs were the best options to control preference bias. And doubly randomised control trials were the most appropriate to evaluate it. Other designs may be of interest to account for caregiver preferences.

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# METHODOLOGY AND PRELIMINARY RESULTS OF A STUDY OF THE ASSESSMENT OF THE ECONOMIC IMPACT OF BALNEOTHERAPY C. Baecher (Nomadeis), C-E. Bouvier (Cneth) (France)

The Observatory of the economy of the thermal spas (OESTh) was launched in January 2020 under the steering of the French Thermal and Climatic Federation (FTCF) and its partners - National Council of the Thermal Establishments (CNETh), National Association of the Mayors of the Thermal Communes (ANMCT), Club of the Thermal Tourist Offices, General Direction of Companies (DGE) and Caisse des Dépôts et Consignations.

It is an innovative project which mobilizes a consequent budget (more than 800 000 € over 6 years) and which benefits from the support of the authorities and public institutions.

#### The Observatory pursues two central objectives:

- to promote the French spa industry and to highlight the positive effects on the development of the territories and the French economy in general, particularly in terms of employment.
- to better know the French spa industry and support the development of the spa economy throughout France.

#### Structuring choices

- an observatory which is going to rely on a wide and cross-cutting vision of the economy of the thermal spas (different types of patients and customers, activities, measurement of the direct, indirect, induced and related impacts).
- a quantitative and qualitative observatory producing indicators at national, regional and local levels. The scoreboard includes 50 indicators divided into 4 main categories:
  - the economic impacts of thermalism,
  - the performance of institutions,
  - the attractiveness of the territories,
  - taxation and local finances of resorts.

The observatory constitutes a major collective project, and will rely on a network of local correspondents for a strong territorial anchoring. 7 regional correspondents and more than 250 local correspondents will ensure that the data is fed back.

#### Duration of the Observatory's mandate: a lasting commitment

The first mandate covers a period of 6 years, from 2020 to 2025, corresponding to the current municipal mandate (firm phase from 2020 to 2022 and conditional phase from 2023 to 2025).

The observatory was launched in 2020 for the first partial results (in 7 pilot spa resorts) in November 2020 and the communication of the first dashboard in November 2021. The presentation focuses on the methodology adopted and the results obtained in the 7 pilot spas resorts.

### SPA DOCTORS : ROLE, PLACE AND RELATIONS WITHIN LES LANDES TERRITORY (FRANCE)

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Keywords: spa doctors, thermalism, Les Landes (France), relationships, institutional logics

The aim of this communication is to highlight the role, place and relationships of spa doctors within Les Landes, one major thermalism territory in France. Data are extracted from the author PhD research presented in October 2017. As cooperation is well known to enable organizations to adapt to evolving environments, the objective of this PhD research was to analyse the ways professional social networks influence cooperation within the competitive thermalism sector in Les Landes.

Preliminary findings indicate that 45 spa doctors in Les Landes are central actors of balneotherapy for this territory. However, the social network analysis revealed that 11 spa doctors participated to the data collection and they declared 31 relationships out of a total of 397 relationships stated by all actors included in the study (thermal spas, local

authorities, regulatory agencies, transports, hotels ....).

Complementary to the limited social network analysis, we draw qualitative data first from 61 interviews with thermalism actors and secondly from observations during 21 events in which spa doctors were involved. These additional results allow us to discuss the place of spa doctors within the thermalism sector in Les Landes. Spa doctors appear to be entrenched in competing institutional logics, health and market logics, which can coexist by means of relationships of cooperation.

This communication contributes to the health / market institutional logics framework by describing the relationships between spa doctors and other actors of the thermalism sector whilst focusing on Les Landes territory.

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# CONSEQUENCES OF GIVING UP ON SPA CARES DUE TO THE PANDEMIC: THE PATIENTS WHO COULDN'T HAVE THEIR SPA TREATMENT IN 2020 EXPRESS A POORER HEALTH STATUTE. DATA OF AN INQUIRY IN 55,000 PERSONS

#### **C-E. Bouvier (Cneth-France)**

#### Context

In the context of the SARS-CoV-2 pandemic, the French thermal establishments were closed as a precautionary measure on 16 March 2020, authorised to reopen on 2 June and then closed again on 29 October. In total, the average operating time was 4 months. 191,000 curists were welcomed in 2020 (i.e. a drop in attendance of -67 %), corresponding to approximately 390,000 curists deprived of their spa care. Many of them spontaneously complained about their poor health condition as the result of their giving up on thermal care. The National Council of Thermal Spas (Cneth), national professional representation of all the French spas, decided consequently to objectify this complaint of the patients deprived of thermal treatments.

The main objective of the study is to evaluate the consequences in terms of individual health of the renunciation of thermal treatments among the persons taking the waters who did not take a cure in 2020. This objective is apprehended through two types of criteria:

- descriptive criteria of the state of health: evolution of pain and symptoms linked to the pathology for which the last treatment was carried out, evolution of the ability to carry out the gestures of daily life, quality of life;
- criteria related to the consumption of health care and medical goods.

#### Method

The Cneth proposed to its members by way of a circular to participate in the online survey "study of the consequences of renunciation of care". Each member was invited to solicit the participation of curists registered in their database, and selected on the following criteria:

• patients who have benefited from a contracted spa treatment (complete or interrupted) in the establishment in 2019 or 2020.

or

- all those who booked their cure in 2020 but did not take it, for whatever reason, and
- whose email address is available and usable in accordance with the General Data Protection Regulation (GDPR).

The questionnaires were collected via the SurveyMonkey online platform over the period from 5 March 2021 to 11 April 2021. In the end, the validated participation rate is estimated at 50,006/435,000, or 11.5 %. The sample constituted is very similar to the data describing the population of curists collected during previous studies.

#### Results

For the purposes of the study, the analysis was based on a comparison between the subjects who underwent their last treatment in 2019 (with and without the intention of undergoing treatment in 2020 – group 1) and those who were actually able to undergo treatment in 2020 (intervention group 2). It turns out that the groups are homogeneous and therefore comparable, with most of the differences between the different modalities being less than 1 %.

The evolution of the subjects'state of health was assessed on the day the questionnaire was filled in, compared to the same date one year before, on the basis of a self-evaluation by the respondent. Taking into account the size of the two samples and thus the law of large numbers, the evolutions of the state of health not linked to the absence of spa treatment (ageing, pathologies, anxious or depressive state induced by the health crisis,...) can be considered as having been neutralised.

The proportion of subjects who declare that their pain and symptoms have worsened or severely worsened is significantly higher in group 1 than in group 2 (exact figures to be disclosed later). The same applies for the ability to perform actions of daily living: climbing stairs, dressing/undressing/grooming, carrying heavy loads, walking, i.e. people with spa cares were better off.

The change from one year ago in the consumption of medicines to treat the condition for which the last treatment was given and the change in the number of consultations with health professionals (doctors, physiotherapists, nurses, psychologists, etc.) compared to a year ago showed that people who had to give up on spa treatments consumed more drugs and other medical services compared to people who could actually maintain their spa treatments.

Although not a clinical study, with answers not corroborated by a clinical examination, this study of patient reported outcomes displays a real robustness which is conferred by:

- its statistical power (more than 50,000 participants).
- external homogeneity (between the sample and the general population of curists) and internal homogeneity (between the control group and the intervention group),
- the magnitude of the differences observed, which largely exceed the level of significance. Moreover, it is such that it makes a more detailed analysis by individual matching and calculation of a propensity score superfluous.

In **conclusion**, the study demonstrates without ambiguity the materiality and the extent of the prejudices undergone by the persons taking the waters deprived of spa treatments, and brings the proof a contrario of the interest of the thermal cure for these populations, so much in terms of individual benefits of health, of quality of life as of collective benefits in terms of reduction of the consumptions of drugs and medical consultations.

# TELE-CONSULTATION AND TELE-INCLUSION: AN OPPORTUNITY FOR CLINICAL RESEARCH IN THERMAL SPA THERAPIES: e-CLINICAL RESEARCH

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Keywords: Teleconsultation, Consent form signature

#### Introduction

The Covid-19 pandemic has disrupted many medical practices and favored the development of teleconsultation. It has also shed light on the structural weaknesses of clinical research, the volume of which has considerably decreased due to the unavailability of investigative physicians. In addition, inclusion consultations and follow-up visits in hospitals and other care structures have been discouraged due to the increased risk of exposing study participants to Covid-19 infection and of outpatients bringing infection into the establishment. All non-Covid clinical trials were therefore suspended for several months.

#### Methods

This context that has led us to find solutions combining respect for Good Clinical Practices (GCP) and teleconsultations for the inclusion visit and follow-up visits: clinical e-research.

Obstacles: The challenges to be met are ethical and regulatory, medical, technical and organizational. Does a teleconsultation allow informed consent in compliance with regulatory texts? How does one obtain the signed written consent, signed both by the investigating physician and by the patient? How does one provide the patient with truly informed consent? What medical information can be reliably collected? Which videoconferencing tools should one choose? What methods of patient recruitment are possible and what organization should one put in place.

#### Results

We have set up the following procedures:

Pre-recruitment of patients directly via the media, social networks and patient associations with dissemination of information to health professionals (doctors, pharmacists, physiotherapists, nurses etc.) to encourage them to talk about the study to their patients.

Information and prescreening by telephone interview with a clinical research assistant. Sending patient information and the teleconsultation procedure by e-mail. Teleconsultations via a dedicated health and secure videoconferencing tool (Sisra developed by the Auvergne Rhône-Alpes region and validated by the Ministry of Health). This tool is accessible via PC, tablet and smartphones. Additional information, oral

agreement from the patient and verification of the inclusion criteria by the investigating doctor in teleconsultation. Data entry and randomization on an electronic case report form (e-crf) website. Signature of the consent with triplicate copies of the consent signed by the doctor sent to the patient. Signature of the 3 copies of the consent form by the patient who returns them to the doctor. Verification by the doctor and return to the patient of one validated copy with the 2 signatures. Planning of follow-up teleconsultation visits.

This organization, which can be described as "e-clinical research", was set up for a study of a home based hydrogen-saturated water treatment of Covid positive patients. Respect of ethical considerations, in particular patient consent, has been validated by a French Committee for the Protection of Persons (CPP). This system is operational and has enabled the inclusion and follow-up of several dozen patients. It has been also approved by an ethics committee (CPP) for the Diabéo2thermes study (Spa therapy for type 2 diabetes).

#### Discussion

The benefits of e-clinical research are obvious. During an epidemic period, this resolves the problem of the risk of contamination for both patients (waiting rooms, hospitals) and caregivers. In order not to impact the overloaded healthcare system, we were able to call in voluntary retired doctors as additional investigators. Outside the context of an epidemic, the main advantage is that the geographical distance between the location of patients and the location of doctors is irrelevant. A doctor can receive patients from all over France in consultation, allowing nationwide recruitment without the need for a large network of investigators, which is very difficult to set up. In particular, this enables clinical research to be extended to include areas with a very low density of doctors (called "medical deserts"). The constitution of a pool of e-clinical investigators trained in GCP not only guarantees the quality of the data and the respect of procedures but also increases the availability of medical investigators, allowing quick appointments.

The reliability of the information gathered during the interview or medical examination poses no particular problem. The possibilities for exchanging documents (results of biological analyses, imaging, hospitalization records etc.) during the teleconsultation complement the consultation very well and make it possible to validate certain criteria. Physiological parameters such as heart rate, respiratory rate and temperature are also easy to collect. Nearly all the elements of a medical examination can be carried out, possibly with the taking and sending of photos. At the end of the teleconsultation, information is immediately transmitted to the patient's GP/primary care physician via a secure messaging server.

Nevertheless, there are important limitations. No clinical signs explored by palpation, such as induced pain are accessible. If the protocol involves clinical maneuvers with specific measures or specialized examinations such as biopsy or other invasive procedures, then a face-to-face consultation is required.

The patient must be able to access teleconsultation and videoconferencing tools. The Covid pandemic has widely popularized videoconferencing, but network coverage

(internet or mobile phone) and the possibility of fast access to multi-media video platforms have not improved (in France), and pose technical constraints. For patients who are less comfortable using IT techniques we have included in the procedures the possibility of asking for help from someone in their entourage.

#### Conclusion

Our experience demonstrates the feasibility of e-clinical research in compliance with ethical and regulatory rules and its very good acceptance by patients.

E-clinical research is particularly well suited to research in thermal spa therapies. Thermal spa resorts are often located in in areas with low population density, which poses specific problems for clinical research. It is very difficult to find physicians, who are both independent of the thermal spas and trained in clinical research, in practice near the resorts to act as investigators to include and assess outpatients. It is also difficult to constitute a national network of investigating physicians motivated by research in thermal spa medicine. In practice, this is most often limited to a few investigators in large metropolitan areas, thus limiting the recruitment pool and excluding entire populations from access to research in thermal spa treatments. E-clinical research, by completely decoupling the patient's location from that of the investigator, solves this type of problem and allows for nationwide recruitment. The chronic diseases treated in a thermal spa are often associated with an active approach on the part of patients in constant search of solutions to relieve their symptoms. This is one of the roles of patient associations and one of the most frequent reasons such patients search for information on the Internet. It is therefore likely that this type of patient is quite receptive to announcements about clinical research projects. The use of a panel of physicians trained in GCP and motivated by research in a thermal spa environment will improve the quality of studies. We hope to demonstrate these points in the "diabéo2thermes" study which, as soon as the thermal spa resorts reopen, will largely rely on an e-clinical research strategy.

### ASSESSMENT CRITERIA FOR CLINICAL TRIALS EVALUATING THE EFFECT OF SPA TREATMENTS IN KNEE OSTEOARTHRITIS (KOA)

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Keywords: knee osteoarthritis; assessment criteria; randomized clinical trial; spa therapy, balneotherapy

#### Introduction

Numerous randomized clinical trials (RCTs) have evaluated the effect of spa treatments in KO. These trials used a wide variety of judgment criteria. It appears necessary to carry out an analysis of the use of these criteria to be able to propose those which appear to be the most relevant for future clinical trials.

#### Methodology

We performed a bibliographic search on RCTs that evaluated the effect of spa treatments in KO from the Medline and Embase databases and from the keywords "knee osteoarthritis", "randomized clinical trials", "spa therapy", "balneotherapy" and "mud therapy". We then researched and analyzed the assessment criteria used in these studies. We also noted the maximum duration of study follow-up.

#### Results

We found 27 RCTs evaluating the effect of spa treatments in KOA.

The assessment criteria used were: a) pain: evaluated by the visual analogue scale (VAS) of pain (26 RCTs), b) function: evaluated by the Western Ontario and McMaster Universities Osteoarthritis Index (Womac) (20 RCTs), the Leguesne AlgoFunctional Index (Lafi) (9 RCTs), the Health Assessment Questionnaire (HAQ) (2 RCTs) and the Knee injury and Osteoarthritis Outcome Score (Koos) (2 RCTs), c) patient's opinion: evaluated by VAS (4 RCTs) or Likert scale (1 RCT), d) quality of life (OoL) (21 RCTs) evaluated by generic questionnaires (SF36 in 9 RCTs, EuroQoL in 5 RCTs, AIMS in 4 RCTs, Nottingham Health Profile in 4 RCTs) or a specific QoL questionnaire for osteoarthritis of the lower limbs (OsteoArthritis Knee and Hip Quality Of Life questionnaire) (OAKHOOL), e) analgesic and/or non-steroidal anti-inflammatory drugs (NSAIDs) consumption (12 RCTs),f) adverse effect (15 RCTs), g) composite criteria as "minimal clinically important improvement" (MCII) (4 RCTs) and "Patient Acceptable Symptom State" (PASS) (2 RCTs). The use of these composite qualitative criteria make it possible to define a yes / no response for each patient [Tubach et al. 2005]. MCII was used as the primary endpoint in 2 RCTs [Forestier et al. 2010, Rat et al. 2020]. It was defined as 19.9 mm or greater on the VAS pain-scale and/or 9.1 points or greater on the Womac function subscale normalised to a 0–100 score and no knee surgery, at 6 months; e) The maximum duration of study follow-up was end of treatments (2 RCTs), 1 month (2 RCTs), 2 months (1 RCT), 3 months (12 RCTs), 6 months (6 RCTs), 9 months (2 RCTs) and 12 months (2 RCTs).

#### Conclusion

KOA is the cause of pain, disability and reduced QoL. Consequently, the most relevant assessment criteria to be used in RCTs evaluating the effect of spa treatments in KO are pain VAS, Womac and Qol questionnaires including a generic questionnaire (EuroQoL or SF36 with a preference for EuroQoL because it appears more sensitive to change) and a specific questionnaire (OAKHHQoL). The use of qualitative composite criteria such as MCII and PASS is also necessary because they are clinically relevant. The assessment of the consumption of analgesics and NSAIDs is needed for the interpretation of the assessment of pain. The evaluation of adverse effects is essential to assess the benefit / risk ratio. Given the persistence of the effect of spa treatments over several months an evaluation follow-up time of at least 6 months to collect these criteria appears relevant.

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### Clinical studies carried out in spa medicine environment within the framework of legal regulations in France.

The Academy of medicine "2016 criteria - 2020 revision"

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Keywords: balneotherapy, spa therapy, natural mineral water, clinical assessment, spa care facility, Academy of medicine (Paris)

People petitioning for the i) opening of a spa care facility, ii) obtaining a new therapeutic orientation (necessary agreement for social security reimbursement), iii) the use of a new spring, iiii) of a new natural mineral water or v) a new treatment have to obtain, through the vote of the plenary National Academy of Medicine, the favorable opinion of the academy.

They will have to produce the 3 following types of study.

- 1° an "analogic study", based on literature data and national experiences and situations, which will have to establish the use of similar mineral waters for comparable purposes and results.
- 2° the "qualitative study" aims to assess the perception by the staff and the patients of the quality, interest, modalities of action of the cares delivered in the facility. Such studies are mainly based on organized verbal inquiries.
- 3° the "clinical studies" must provide proofs of clinically convincing therapeutic efficacy. In all cases, these last studies should lead to a valid comparison of the implemented treatment. This comparison can be made with existing data, in particular randomized controlled trials considered to be a robust reference. The comparison should be made on individual data and not on aggregates of data. Match Adjusted

Indirect Comparison (MAIC) techniques are appropriate. Where data allowing this type of comparison are not available, randomized controlled trials are the rule however Bayesian clinical trial techniques, which provide valid data from a limited number of patients, can be considered.

Furthermore, all scientific and ethical rules of clinical investigation must be observed.

These new criteria have been accepted by the vote of the Academy on 8<sup>th</sup> December 2020 (ballot results: yes 110 votes, no 5 votes).

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## ACTUAL MEDICAL BENEFIT CANCER - DERMATOLOGY

### POST-CANCER SPA THERAPY: EVALUATION OF THE KNOWLEDGE AND EXPECTATIONS OF PHYSICIANS AND PATIENTS IN A CANCER CENTER

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Keywords: crenobalneotherapy; spa therapy; cancer; supportive care

#### Introduction

Advances in cancer treatment have helped to reduce cancer-related mortality. The experience of the disease remains a difficult experience due to the side effects of the treatments and has an impact on "after cancer" life. It has been shown that 63.5 % of patients suffer from after-effect 5 years later: changes in self-image, pain, fatigue... These after-effects are not subject to specific medical follow-up in 75 % of cases [1]. Since the 1990s, French cancer physicians developed supportive care, defined by the "Association Francophone pour les Soins Oncologiques de Support" (www.afsos.org) as "all the care and support necessary for patients throughout the course of the disease, in conjunction with specific treatments when available". Through the national cancer plan, the French government has set objectives for professionals to provide access to supportive care throughout the country, to reduce the health consequences and the risk of a second cancer [2]. French spas offer "post-cancer" programs that combine hydrotherapy with health education and rehabilitation support. The Pacthe prospective multicenter randomized controlled trial, conducted on 270 women in remission from breast cancer, compared a "spa group" benefiting from a 13-day full-board stay in a spa with interventions combining hydrothermal treatments, adapted physical activities, dietary meals and nutritional education, aesthetic treatments, and psychological support, to a "control group" of women benefiting from usual hygienic and dietary monitoring by their referring physician. The trial showed an improvement in quality of life, depression, sleep quality, physical activity level and weight control in the spa group [3].

The objective of this work is to evaluate the knowledge and expectations concerning the post-cancer spa therapy of the oncologists of a French Comprehensive Cancer Center (Godinot Institute, Reims, France) and of the patients who are treated and followed there.

#### Methods

The survey was conducted using two questionnaires.

1) The physician questionnaire was designed on Survey Monkey and sent by email to 24 physicians: 12 chemotherapists, 7 radiotherapists and 5 surgeons, on September 14,

- 2020 with a reminder at day seven. It included 3 items about "classic" spa therapy not related to cancer and 9 items about post-cancer treatments (knowledge of the treatments and spa resorts involved, indications, treatment, reimbursement, research work carried out on the subject, advice and/or previous prescriptions, information or training needs).
- 2) The patient questionnaire was given out in paper form at the reception desk to 280 outpatients from 14 to 16 September 2020. The general items were gender, age and type of cancer. Eight items concerned post-cancer spa therapy: knowledge of this treatment, the resorts concerned, indications, prescription and health insurance reimbursement. For those who already had a spa treatment: name of the resort and indication. For those who had no spa experience: interest, preferred physician to discuss it, expected benefits in order of preference from a list of 12 proposals, resort considered in the region or elsewhere.

#### Results

#### Physician responses

The participation rate of physicians was 42 % (10/24): 6 chemotherapists, 3 radiotherapists, 1 surgeon. All knew about the existence of post-cancer spa therapy: 4 from patients, 3 from colleagues, 1 from the press, 2 from another intermediary, none from internet networks. Three out of ten knew of at least one resort that offered spa therapy, the only resort cited was La Roche Posay. Eight out of ten knew the indications and cite fatigue, post breast cancer, skin sequels, lymphoedema and pain. Two out of ten knew the prescription procedure, none the reimbursement conditions. Five out of ten have already recommended spa therapy, one has already prescribed it. Seven physicians said that conventional spa therapy was not interesting, while 9 thought that post-cancer spa programs were of quite or great interest. Only one radiotherapist was aware of any research on post-cancer spa treatments. The expected means to better talk about it to the patients are a short formation on the subject (3/10), a practical guide on the subject (6/10), a doctor of the institute trained in spa therapy to refer the patient (6/10).

#### Patients responses

The patients participation rate was 71 % (200/280 questionnaires distributed). Age ranged from 50 to 70 years for 59.5 %, less than 50 years for 15.5 % and more than 70 years for 25 %. Women represented 70 % of the respondents (140/200) and breast cancer 48.5 % (97/200). Post-cancer spa therapy was known by 13 % of respondents, the resorts offering them by 4.5 % and the indications by 4 %. The procedures to follow to request a post-cancer spa treatment were known by 4.5 % of respondents, and reimbursement by the health insurance by 3.5 %. Two patients have previously benefited from a post-cancer spa therapy at La Roche Posay, 56 % (112/200) of respondents said they were interested and would like to discuss about it with their oncologist for 33 % of them and with their family doctor for 22 %. Those interested in post-cancer treatments represent 61 % (86/140) for women and 43 % (26/60) for men. Interest varies according to the type of cancer: 65 % (63/97) of those followed for breast cancer, 36 % (9/25) for urological

cancers, 55 % (10/18) for head and neck cancers, 59 % (10/17) for digestive cancers, 35 % (6/17) for gynecological cancers, 67 % (8/12) for pulmonary cancers. For all, whatever the type of cancer, the first expected benefit is to regain "overall physical and mental well-being". Particularities are then distinguished according to the type of cancer: recovery of better sleep and correction of weight gain for breast cancer; reduction of sexual disorders secondary to treatment in urological cancers; reduction of anxiety-depression in head and neck and lung cancers; recovery of better mobility for digestive cancers; reconstitution of self-image and self-esteem in gynecological cancers. To the question: in which region would you do the post-cancer treatment, the answer is "rather away from home so that it is also an opportunity to discover another region" for 38.5 % (77/200), nearby "in a resort in the region" for 33 % (66/200), and 28.5 % (57/200) do not know. A practical guide to post-cancer treatments would be of interest to 63 % (126/200) of respondents.

#### Conclusion

This study shows that all the oncologists at the Godinot Institute in Reims are aware of the post-cancer care offered by the spas and show a definite interest in these specific treatments. They limit the indications to post-cancer of the breast, skin after-effects, lymphoedema, pain and fatigue. Due to insufficient knowledge of the procedures for prescription and health assurance reimbursement, one physician out of two declares having already recommended spa therapy, only one has prescribed it. Physicians are not aware of research in this field. The survey highlights the need for information, continuing education and sharing of experience between cancer and spa professionals.

The participation rate of patients in the survey is high. Although few patients were aware of the existence of post-cancer spa therapy and the practical procedures involved, 56 % said they were interested: more than one in two patients with breast, head and neck, digestive or lung cancer. Particularities appear in the expected benefits depending on the type of cancer. While post-cancer programs today mainly target women in remission from breast cancer, this survey shows that patients with other cancers are also looking for specific support. The main doctor to talk to about this is the oncologist.

Spa therapy appears to be an original offer in support care for post-cancer in the framework of the personalized post-cancer programs. The answers given by doctors and patients converge towards the need for information and training of health professionals in oncology so that they can in turn offer these specific treatments to people suffering from post-cancer sequels.

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# "PACTHE" PROGRAMME FOR ACCOMPAGNYING BREAST CANCER PATIENTS IN SPAS AFTER COMPLETION OF CANCER TREATMENT: RESULTS OF A RANDOMIZED TRIAL ON 251 PATIENTS

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Key-Words: breast cancer; QoL; spa treatments; physical activity; health education

#### Introduction

Quality of life is greatly impaired in women just after the completion of the surgery-chemotherapy-radiotherapy sequences for the treatment of their breast cancer. Most of the women present transient depression symptoms in the few months following their treatment although in complete remission of their cancer. Neither hospital nor home is well adapted for helping the women in this period of difficulties.

Many studies demonstrate that high body mass index (BMI) at breast cancer diagnosis is related to relapse risk and impaired the survival prognosis. Moreover, adjuvant chemotherapy is significantly associated with weight gain, which itself is related to increased mortality of breast cancer. More than one half of women showed a weight gain of 2,5 to 5 kg, when adjuvant chemotherapy regimen is applied. Each 5 kgs gain induces an increased of 12 % of overall mortality, 13 % of breast cancer mortality and 19 % of cardio-vascular mortality. Physical activity is known to have a protective effect against breast cancer risk and against breast cancer relapse although about 75 % of breast cancer patients are inactive.

#### **Hypothesis**

Multidisciplinary health care in spas might improve quality of life and help increasing physical activity and avoiding weight gains in women just after the completion of their breast cancer treatment (within 6-9 months).

#### **Objectives**

*Main objective* : long-term improvement of the quality of life scores of women. *Secondary objectives* 

- avoid weight gain, reduce overweight in high BMI women,
- increase physical activity to the international recommendations.
- Evaluate the cost-effectiveness of the spa treatment.

#### Method

A randomized clinical trial was developed with 2 arms for women with a medical certificate of complete remission of their breast cancer: first arm with individual standard recommendations (stressless activities, nutrition, physical activity) and follow-up of women every 6 months at home, second arm with 10-women-groups in an intensive multi-disciplinary spa course of education of protective nutritional and physical activity for two weeks in a complete pension (in one of three spas in the region Auvergne in France: Vichy, Châtel-Guyon, Le-Mont-Dore). Randomization is made before the ninth month after completion of the chemotherapy/radiotherapy/surgery sequence. Only one spa course was organized per woman.

During the 2 weeks-thermal stay, a personalized programme is set up with:

- individual consultations with physician, nutritionist, physiotherapist and psycho-oncologist,
- nutritional education: adapted menus in complete pension at the hotel according to the WCRF recommendations, cooking workshops, seminars,
- 2 physical accompanied physical activities per day with a progressive increasing intensity programme according to the basal capacities of each patient,
- 4 spa treatments every day,
- esthetical cares, individual relaxations,
- shoulder mobilisation.

Every 6 months, patients had a medical consultation (oncology, anthropometric measurements) and questionnaires (SF36, physical activity, sedentary lifestyle, sleep quality, HAD), to fill out for 2 years, then annually for 3 years.

#### Results

198 eligible women declined the PACThe program (mainly for personal reasons, secondly for comorbidity), 251 accepted, 117 were randomized in the "spa" arm, 116 in the control arm. There no discordance in medical cares or results between the 3 spas.

- Average age : spa group:  $52.14 \pm 9.02$  yrs; control group  $52.40 \pm 10.14$  yrs
- Average BMI : spa group:  $26.03 \pm 4.57$ ; control group  $25.36 \pm 4.15$ . 54 % of women were overweighed at the start of the program.
- At 2 years: Control group gained weight (non significant) and spa group lost weight compared to control group, with a significant difference between the two curves (p = 12x 10-6) and a weight differential of 2.2 % at 1 yr and 1.5 % at 2 years. The two curves merged at 3 years. At 2 years, the waist size decreased in spa group (significant difference

between the two curves with p < 10-7), and impedancemetry showed significant less fat mass (p= 11x10-4) and more lean mass (p= 28x10-4) in the spa group.

- 55 % of patients were inactive at the start of the program. Physical activity level remained stable in control group and significantly increased in the spa group (p=0,004) at one year and at 2 years (14 % more women are physically active in the spa group compared to control). No difference was observed after 3 years. No significant evolution of sedentary score was observed in both groups.
- Anxiety is only transiently improved at 6 months in spa group but not at one year. On the other hand, depression is significantly improved in the spa group ( $p=7 \times 10-5$ ) at 2 years but not later. Sleep quality has been significantly improved in the spa group (difference between the two curves p=10-4) for 3 years.
- All along the 5 years survey, the quality of life (QoL) is significantly higher in the spa group compared to the control group (difference between the two curves p=10-6) in both physical and psychological items. QoL increased non-significantly in control group for 2 years.

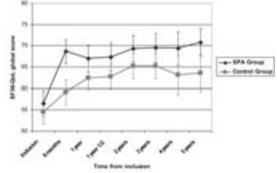


Fig 1: 5-years compared SF36 scores (QOL) between spa & control groups. (p=16x10-4), a higher rate of resumption of activities (p=25x10-4) at one year (professional activities with p=14x10-4, familial activities with p=0.033).

#### Conclusion

With the improvement of cancer treatments, QoL after breast cancer complete remission is becoming a challenge for oncologist and physicians. PACThe is the first demonstration of a long-term (over 5 years) improvement of the quality of life (QoL) by a medical intervention. Accompanying women after completion of their breast cancer treatment might be recommended for improving their QoL with a 2-weeks spa and educational program. Moreover women testify psychological improvement like "to be able to devote time to find myself" or even to be "resurrected" after the PACThe program.

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# EFFICACY AND TOLERABILITY OF BALNEOTHERAPY ON SKIN COMPLICATIONS AFTER BREAST CANCER SURGERY AND RADIOTHERAPY:

#### RESULTS OF A RANDOMISED, CONTROLLED, OPEN-LABEL TRIAL

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#### **Introduction & Objectives**

Secondary skin complications are common after breast cancer treatment. The primary objective of this trial was to evaluate the efficacy of balneotherapy on skin xerosis observed in patients treated for breast cancer by surgery (with or without chemotherapy) and radiotherapy.

#### Material & Methods

A multicentre, open-label, randomised, controlled trial was conducted in patients who had skin xerosis of grade ≥5 (on a visual analogue scale [VAS] from 0 [no dry skin at all] to 10 [extremely dry skin, worst ever]) at inclusion within 8 weeks after post-operative radiotherapy for breast cancer. Patients were randomly assigned (1:1) to follow 18 consecutive days of La Roche Posay post-cancer dermatological balneotherapy within 12 weeks after the end of their radiotherapy (balneotherapy arm) or usual care for 36 weeks with deferred balneotherapy after the end of the study (control arm). The primary endpoint was patient-assessed skin xerosis measured by VAS. Secondary endpoint assessments included investiagtor-assessed xerosis by scaling, roughness, redness and cracks (SRCC) score, Vancouver surgical scar characteristics score, neuropathic pain diagnostic score (DN4), patient-assessed pain (VAS) and QLQ-C30 global health status/quality of life with BR23 module arm symptoms score.

#### Results

Between 2014 and 2018, a total of 128 patients were randomised and 109 completed the study. Xerosis improved in the balneotherapy arm from the first evaluation visit 7 days after the balneotherapy with a mean VAS score of 2.0 ( $\pm$  1.7) compared to 6.1 ( $\pm$  1.5) at baseline. At the final visit (36 weeks after radiotherapy), the mean VAS for xerosis was significantly better for patients in the balneotherapy arm *versus* the control arm (2.0 [ $\pm$  2.5] *versus* 3.5 [ $\pm$  2.4]; p=0.001), corresponding to mean percentage reductions from baseline of 70 % and 43 %, respectively. More patients in the balneotherapy arm had a reduction of more than 30 % in their skin xerosis VAS score between baseline and final visit than in the control arm (82 % *versus* 65 % of patients, respectively; p=0.053). At the final visit, improvements in favour of the balneotherapy arm were observed for mean SRCC score (0.8 [ $\pm$  2.5] *versus* 1.8 [ $\pm$  2.2]; p=0.0001), as well as for Vancouver score, pain, global health status/quality of life, and arm symptoms. Overall, 40 patients had a total of 72 adverse events; only 2 events (breast oedema and musculoskeletal pain) were considered as being related to the study treatment.

#### **Conclusions**

Balneotherapy demonstrated rapid and sustained efficacy on skin xerosis from postoperative radiotherapy for breast cancer, as well as improvements in pain, neuropathic pain, global health status/quality of life and arm symptoms.

# EVALUATION OF THE BENEFIT OF THERMAL SPA TREATMENT IN PLAQUE PSORIASIS: THE PSOTHERMES MULTICENTRE, OPEN-LABEL, RANDOMIZED CLINICAL TRIAL

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Keys words : Thermal Spa, Balneotherapy, Psoriasis, Quality of Life, Dermatology Life Quality Index

#### Introduction

Psoriasis is a chronic inflammatory skin disease, challenging due to its chronicity, with a negative effect on quality of life (QoL) and a high prevalence of comorbidities. In recent years, important therapeutic advances have improved the management of moderate to severe psoriasis. The choice of treatment depends on the patient's and disease's characteristics and in a single patient, it may be necessary to use different successive lines of treatment throughout life in this chronic disease (Nast et al. 2020). In patients with limited disease, who represent the majority of the psoriasis population, topical drugs are the first line treatment, but can be burdensome and they associated with poor adherence. Thermal Spa therapy is mostly considered as an add-on treatment for psoriasis: complementary or as a pause between treatments. However, it suffers from the absence of objective evaluation in absence of multicenter randomized trials [Cacciapuoti et al. 2020].

The aim of our study was to assess the early and long-term benefit of spa treatment focusing on QoL but also on other criteria such as pain, itching and psoriasis severity.

#### Methods

Psothermes was a multicentre, open-label, randomized trial, comparing immediate versus delayed spa treatment 4.5 months later (NCT02098213). Spa therapy was conducted in five French spa resorts (St Gervais, La Roche Posay, Molitg, Avène and Uriage). Procedures during the spa therapy were standardized after a prior consensus between the participating thermal spa centres. They consisted in 18-day dermatology-oriented course of spa therapy including filiform showers, balneotherapy in a pool, full

body and facial sprays and localised treatment. In addition, participants attended educational workshops. Inclusion criteria were: adults with plaque psoriasis, Dermatology Life Quality Index (DLQI) > 10, and stable medical treatment in the last 6 months. Primary outcome was improvement of DLQI  $\leq$  10 at 4.5 months after inclusion. VQ Dermato and EQ5D-3L also assessed quality of life (QoL), Perceived Stress Scale (PSS) stress, and visual analogue scales (VAS) pain and pruritus. Psoriasis clinical improvement was assessed unsing the PASI. Dermatologists in charge of inclusion and were independent of the spa stations and had been recruited mainly through the French Psoriasis Research Group of the French Society of Dermatology.

#### Results

Between January 2015 and November 2018, 128 patients were randomised. Among 110 with main endpoint at 4.5 months: 57 received immediate spa therapy (median time after inclusion: 34 days) and 53 received delayed spa therapy after measurement of endpoints at 4.5 months. Most were first-time spa users (71.2 %). Mean DLQI and Psoriasis Area and Severity Index at inclusion were 16.7 and 10.5, respectively.

Intervention Group	Inclusion	4.5 months	6 months	9 months	12 months
DLQI, mean [95%CI]	16.6 [15.5-17.7] n=64	9.5 [7.8-11.1] n=59	8.2 [6.6-9.9] n=56	8.5 [6.9-10.1] n=50	7.7 [6.1-9.4] n=54
V-Q Dermato, mean [95%CI]	67.2 [64.2-70.3] n=59	44.8 [39.3-50.4] n=55	40.9 [34.8-47.1] n=52	42.4 [36.0-48.8] n=47	40.7 [34.5-46.8] n=49
pruritus VASt, mean [95%CI]	6.7 [6.1-7.3] n=64	4.3 [3.6-5.0] n=59	4.1 [3.3-4.8] n=55	4.3 [3.5-5.0] n=50	3.6 [2.9-4.4] n=53

The immediate spa therapy group achieved the primary objective in 66.1 % [95 % CI 52.6 % > 77.9 %] of patients vs 41.4 % [95% CI 28.6 % > 55.1 %] in the delayed group (p=0.007). The proportion of patients with a decrease of at least 5 points in their DLQI score at 4.5 months (compared with their score at inclusion) was 72.9 % in the intervention group versus 46.2 % in the control group (p=0.004). VQ Dermato score and pruritus VAS significantly improved. Conversely, no significant difference was found concerning the VAS pain estimation, the overall quality of life measured by the EQ5D-3L questionnaire, the clinical evaluation of psoriasis measured through the PASI, or stress evaluated using the PSS scale (Table 1). Outcomes at 12-months follow-up of immediate spa therapy group showed persistent improvement of DLQI, VQ-Dermato and pruritus (Figure 1). All the results were comparable whatever the thermal spa centre, the severity of the psoriasis and the naı̈ve/returning curist status of the patients

<b>Table 1</b> . Primary and see	condary endpoints
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		Intervention group	Control Group	p-value
Primary endpoint				
DLQI ≤ 10 at 4.5 months*, n/N (%)		39/59 (66.1)	24/58 (41.4)	0.007
Quantitative secondary endpoints	month			
V-Q Dermato, mean (SD)	0 4.5	67.2 (11.6) n=59 44.8 (20.6) n=55	65.2 (16.1) n=54 56.1 (20.1) n=45	0.003
Pruritus VAS, mean (SD)	0 4.5	6.7 (2.4) n=64 4.3 (2.7) n=59	6.8 (2.5) n=61 5.4 (2.8) n=50	0.047
Pain VAS, mean (SD)	0 4.5	4.1 (2.8) n=64 2.9 (2.8) n=59	3.7 (3.1) n=61 3.0 (2.9) n=50	0.309
EQ5D-3L index, mean (SD)	0 4.5	0.57 (0.27) n=64 0.69 (0.27) n=59	0.61 (0.29) n=61 0.66 (0.30) n=51	0.191
Perceived stress: PSS 14, mean (SD)	0 4.5	27.8 (7.1) n=64 24.9 (7.1) n=59	27.2 (6.9) n=61 25.4 (9.0) n=52	0.498
Qualitative secondary endpoints				
V-Q Dermato ≤ 35 at 4.5 months, n/N (%)		17/55 (30.9)	8/45 (17.8)	0.131
PASI75 at 4.5 months, n/N (%)	_	8/56 (14.3)	5/53 (9.4)	0.435

<sup>\*</sup> after replacement of missing values DLQI: Dermatology Life Quality Index; EQ5D-3L:

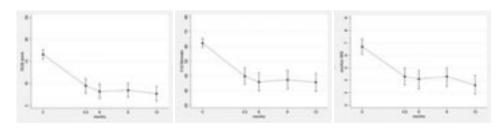


Figure 1: Long-term assessment in the intervention (immediate spa therapy) group

#### Conclusion

This RCT demonstrated that a cure of spa therapy improves QoL as assessed by specific dermatological disease scores : DLQI and the VQ-dermato scores, as well as pruritus, in

short and long-terms (12 months). These results justify the integration of balneotherapy in the therapeutic strategies for psoriasis. It remains to be determined, which is the adapted patient profile who would gain most benefit from spa therapy.

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Funding: Afreth (Paris, France)

## MOLECULAR MAPPING OF SODIUM SELENITE TARGETS IN NORMAL HUMAN KERATINOCYTES

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The goal of this study was to perform a global mapping of the molecular effects exerted by physiological amounts of selenium on human keratinocytes. To achieve our goal, primary cultures of human keratinocytes were subjected to 24h stimulation with sodium selenite (NaSe) at doses that i) do not impact cell survival and ii) are similar to the concentrations observed in selenium-rich spa waters. Irrespective of the condition tested, we found that more than 2 154 proteins were abundantly expressed by cultured human keratinocytes, as assessed by liquid-chromatography mass spectrometry (LS-MS). These highly expressed proteins comprised one selenoprotein, Thioredoxin

reductase 2 (TXNRD2), and its substrate, Thioredoxin (TXN), Using LS-MS, we identified 3 proteins exhibiting statistically significant quantitative changes following NaSe stimulation: the endosomal protein RAB9A9, the RNA helicase DDX42 and, interestingly, the NAD(P) mitochondrial transhydrogenase (NNT also known as nicotinamide nucleotide transhydrogenase). Indeed NNT plays a key role in mitochondrial oxydo-reduction enzymatic reactions in which TXNRD2 is involved. To further map the molecular targets of NaSe in human keratinocytes, RNA-seq analyses were performed on control vs NaSe-stimulated cultures of human keratinocytes. This approach allowed identifying 12 578 mRNA species with expression levels above the detection threshold in all analyzed samples. From these mRNA species, 11 encoded selenoproteins (among which TXNRD2 and TXN) and 52 were differentially expressed in NaSe-stimulated keratinocytes. Of note, 5 genes coding for selenoproteins exhibited increased mRNA levels under conditions of NaSe stimulation: TXNRD1, TXNRD2, GPX1, GPX3 and SEPW1. Moreover, in the co-expression network linking genes which expression is stimulated by NaSe, TXNRD1 was found to be the main hub gene. However, among the 5 selenoproteins-encoding genes which mRNA levels are increased by NaSe stimulation, only the mitochondrial and cytoplasmic selenoprotein GPX1 exhibited a parallel increase in protein expression, as assessed by western blot. Overall, our results demonstrate that in human keratinocytes, low concentrations of NaSe are able to target several oxydo-reduction enzymatic reactions involving.

Funding: Afreth (Paris, France)selenoproteins with cytoplasmic and/or mitochondrial localization.

#### MUSCULO-SKELETAL CONDITIONS

## SPA THERAPY FOR THE TREATMENT OF FIBROMYALGIA: AN OPEN, RANDOMIZED MULTICENTER TRIAL

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Keywords: Fibromyalgia; Spa Treatment; Pain Measurement; Patient Satisfaction; Treatment Outcome

#### Introduction

Fibromyalgia is the most frequent chronic pain pathology with an incidence of 4.3 per 1000 person-years. The physiopathology is not fully understood and there are no specific somatic signs. The International Association for the Study of Pain (IASP) and American College of Rheumatology (ACR) define fibromyalgia as chronic widespread pain, lasting for at least three months, without any apparent tissue damage or inflammation [1]. The heterogeneous symptoms and poorly understood pathogenesis makes treatment for patients with fibromyalgia challenging [2,3]. The European League Against Rheumatism (EULAR) evidence-based guidelines recommend personalized management with a graduated approach adapted to the symptoms of fibromyalgia, shared decision-making, and non-drug therapies as first-line treatment [4]. Physical exercise was the only non-drug therapy with a 'strong' recommendation and other non-drug therapies, including spa therapy, had 'weak' recommendations.

Several literature reviews have concluded that spa therapy could provide a small overall improvement in pain and health-related quality of life in patients with fibromyalgia, at least in the short-term, but the evidence is weak, particularly for long-term benefits [5-12]. Therefore, high-quality studies assessing long-term maintenance of the beneficial effects with larger sample sizes are needed to confirm the therapeutic benefit of spa therapy.

#### Methods

An open, randomized clinical trial of patients with fibromyalgia comparing an immediate *vs* delayed 18-day spa therapy in five spa therapy care facilities in France enrolled 220 patients.

Patients were recruited throughout France, either during a consultation with a participating pain or rheumatology specialist (n=11) in private practice or hospital.

Randomization was in blocks of four, stratified by center, severity of fibromyalgia and previous spa therapy. The patients were randomized to immediate spa therapy (intervention group) or to delayed spa therapy (control group). The patients in the immediate spa therapy group received a 3-week spa therapy within six weeks of inclusion. The patients in the delayed spa therapy group followed their usual treatment up to the 6-month follow-up visit when the primary outcome was evaluated. Then they received their 3-week spa therapy. This group was considered as the control group, since the primary outcome was evaluated at the 6-month follow-up visit before they had received the intervention. All patients were evaluated at baseline and followed-up at 3, 6, 9 and 12 months.

The primary endpoint was the percentage of patients with a minimal clinically important difference (MCID) defined as a decrease of more than 14% in their FIQ score at 6 months compared with inclusion [13,14].

#### Results

Between September 2014 and September 2017, more than 400 patients were preselected and 220 patients were randomized to the immediate spa therapy (intervention) or

delayed spa therapy (control) groups. Follow up was completed in October 2018. The intention-to-treat analysis included 100 and 106 patients in the intervention and

control groups, respectively.

At 6 months, 45/100 (45.0 %) and 30/106 (28.3 %) patients in the intervention and control groups, respectively, achieved a MCID (p=0.013). There was also a significant improvement in pain, fatigue, and symptom severity (secondary outcomes) in the intervention group (Table 1). There is no significant improvement for generic quality of life (QOL), sleep or physical activity. None of the 33 serious adverse events reported by 25 patients were related to the spa therapy.

Table 1. Primary and secondary endpoints with a significant improvement

		Control group	Intervention group	p value*
Primary endpoint			-	
MCID at six-months, n/N (%)		30/106 (28.3)	45/100 (45.0)	0.013
Secondary endpoints				
Drie WAR (diese)	M0	59.6 ± 14.0 n=96	$61.4 \pm 17.1  n=93$	
Pain VAS (diary),	M3	$58.7 \pm 20.1  n=95$	$54.4 \pm 22.0  n=91$	0.013
mean (± SD) n	M6	$58.9 \pm 21.0 n{=}78$	$53.5 \pm 22.3  n=83$	
101 101 1 1 1	M0	$13.8 \pm 2.8  n = 108$	$14.3 \pm 3.0  n=110$	
Widespread Pain Index Score,	M3	$13.1 \pm 3.7  n=102$	$11.4 \pm 4.3  n=93$	< 0.001
mean ± SD n	M6	$13.2 \pm 3.7  n=96$	$11.8 \pm 4.5  n{=}90$	
	M0	26.2 ± 4.2 n=103	25.3 ± 4.7 n=105	
Pichot's Fatigue Scale Score,	M3	$25.2 \pm 4.6  n = 100$	$22.4 \pm 5.8  n = 90$	0.014
$mean \pm SD n$	M6	$25.2 \pm 4.8  n = 98$	$22.9 \pm 5.7  n=91$	
	MO	9.8 ± 1.6 n=108	$10.0 \pm 1.5  n=110$	
Compton Consist Costs Con-	M3	$9.4 \pm 2.0  n=102$	$8.8 \pm 2.1  n=93$	
Symptom Severity Scale Score, mean $\pm$ SD $n$	M6	$9.5 \pm 1.8  n{=}96$	$9.0 \pm 2.1  n{-}90$	0.002

<sup>\*</sup> p-value for the comparison between intervention and control groups at 6 months. FIQ: fibromyalgia impact questionnaire; HADs: Hospital Anxiety and Depression Scale; MCID: Minimal Clinically Important Difference on FIQ:

#### Conclusion

A 12-month, open, randomized clinical trial of 220 patients with fibromyalgia compared an immediate vs. delayed (i.e. after 6 months) 18-day spa therapy. The results demonstrate the benefit of spa treatment in patients with fibromyalgia with a clinically significant improvement at 6 months for those who received immediate therapy which was maintained up to 12 months.

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## BALNEOTHERAPY AND FIBROMYALGIA: THE EVIDENCE OF THE LAST 5 YEARS IN REVIEW

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Keywords: Balneotherapy, Spa Therapy, Water-based, Fibromyalgia

#### Introduction

Fibromyalgia is a disorder that accounts for the most common cause of widespread musculoskeletal pain. Often present are other symptoms that include fatigue, depression, psychiatric disturbances and somatization [1] with some conditions such has irritable bowel syndrome and migraine clustering in these patients. It is a controversial condition, where patients often look well, with no obvious alterations on the physical examination other than tenderness in soft tissue. Laboratory and radiological studies are also usually normal [1]. Initially it was considered a psychosomatic, but nowadays, with ongoing research, it is thought to be a disorder of pain regulation with central sensitization [2]. Woman between the ages of 20-55 years are the most affected, with a prevalence of 2-3 % that increases with age [3-4]. Fibromyalgia can be challenging to treat, with the need to apply multidisciplinary and individualized regimens to each patient, using pharmacological and non-pharmacological approaches. On the non-pharmacological side, balneotherapy offers an interesting alternative, with a 2014 review by Naumann et al. [5] showing a moderate evidence of a medium to large effect of BT on trigger point count (TPC), medium effect on HRQoL and no significant effect on Beck's Depression Index (BDI). This review confirmed the results of 2 previous reviews [6-7], although stated that the sample sizes were small and there was a risk of overestimation. So, has there is a need for more data to confirm the benefits of BT in the fibromyalgia setting, we aimed to review the literature published from 2015 forward, to assess the efficacy of this therapeutic modality.

#### Methods

An electronic search of databases was conducted (PubMed and PEDro) from the year 2016 forward. The keywords used were: balneotherapy, spa therapy, water therapy,

fibromyalgia and FMS. Keywords were combines using Boolean operators. The articles found were screened by the title and abstracts, to assess if balneotherapy was the main treatment. Those selected were read in their entirety for inclusion on this review.

#### Results

Of the search made, 52 articles were found. After excluding duplicates and non-relevant papers, a total of 20 had their abstracts analyzed. A total of 11 studies were fully read, with 4 excluded at this point for not meeting the criteria, with 7 papers included on this review. As for the type of study, 4 were RCTs, 2 observational studies and one was a case-control study. 6 studies conducted the therapy using mineral water, with different temperatures and compositions, and one used mud baths. One study also incorporated the effects of aerobic exercise (AE). Pain was assessed in all studies using various methods: Visual Analogic Scale (VAS) [8,10-12,14], Trigger Point Count (TPC) [12], Widespread Pain Index (WPI) [10] and Allodynia [9] and Total myalgic score [13]. All studies showed a significant reduction of pain, comparing with baseline values and the controls used in them, with long-lasting effects.

Fibromyalgia impact questionnaire (FIQ) was evaluated in 6 articles and in all of them it was significantly reduced with BT, not only compared to baseline but also comparing with the controls, and with long-lasting effects. Mental wellbeing was surveyed in 4 studies [8,10,11,13] using Beck Depression Inventory (BDI), State-trait Anxiety Inventory (STAI) and Center for Epidemiologic Studies Depression Scale (CES-D). All studies showed an improvement of mental well-being in FM patients with BT at all follow-up points, all three that used BDI for assessment [8,11,13] and the CES-D score on the other one [10]. Anxiety, measured with STAI was no significantly changed [10]. Three papers studied the impact on the overall health [8,10,11] using Short Form 36 (SF-36) [8], Short Form Health Survey (SF-12) [10], Fibromyalgia Severity Scale [8], Symptom Severity Score (SS) [10], Patient General Evaluation and Physician General Evaluation [11]. All of the papers showed an improvement in overall health perception, but not at all follow-up points of evaluation [10]. Fatigue [12], sleep quality [13], were evaluated by one study each, with improvements being reported. Biochemical studies and Hematologic studies were performed in one study [14], with some parameters showing improvement, while others worsened. The impact of BT on the use of pharmacological agents was evaluated in one study, with no differences being reported [9].

#### Conclusion

Many previous reviews studies regarding the effect of BT on fibromyalgia, suggested a positive impact on this disorder, but all mentioned the need for better studies and more evidence regarding the effectiveness of such approach. All studies reviewed here showed a positive impact of BT in fibromyalgia patients, with some reporting long-lasting effects, with improvement of pain, impairment and depression symptoms. This study helps support the use of BT in this setting, compounding more evidence on the positive effects of this non-pharmacological approach.

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#### THERAPEUTIC PATIENT EDUCATION FOR FIBROMYALGIA DURING SPA THERAPY: A RANDOMISED CONTROLLED TRIAL

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Keywords: Fibromyalgia; Pain; Therapeutic patient education; Fibromyalgia impact questionnaire; Randomized controlled trial

#### Introduction

Fibromyalgia is a chronic painful condition affecting about 1.6 % of the population in France, mostly middle-aged women. The central nervous system is involved but mechanisms are still unclear, and symptoms are non-specific. Disease impacts are both phy-sical and psychological, with strong limitations in domestic, professional and leisure activities

Management is complex. The European Alliance of Associations for Rheumatology (Eular) recommends some drugs (analgesics, anti-epileptics, anti-depressants...) despite their limited efficacy, and non-drug therapy (physical exercise, physiotherapy, hydrotherapy, acupuncture, mind-body techniques...) [Macfarlane et al, 2017]. Spa

therapy and its analgesic and relaxing effects has an effect size of 2.1 on fibromyalgia impact and 1.4 on pain [Carville et al., 2008].

Whatever the disease, therapeutic patient education aims at improving knowledge on disease and its management, and life habits. We proposed a therapeutic patient education program during spa therapy, to take advantage of the patient's physical and mental availability during this special period.

#### Methods

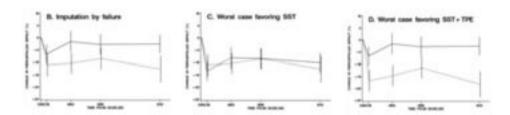
FiETT was a phase III, superiority, randomised, open label trial in two parallel arms among fibromyalgic patients during a 3-week fibromyalgia-specific spa therapy in Dax resort. It compared standardised spa therapy (SST) to SST plus therapeutic patient education (SST+TPE). Outcomes were collected by eCRF during spa therapy (visits at D00, D09, D18), or remote follow-up when patients were back home (self-questionnaires at M03, M06, M12). The primary outcome was the mean score on Fibromyalgia Impact Questionnaire (FIQ) at M06. The primary analysis was on intent-to-treat with missing FIQ replaced by failure (first decile observed in the same arm). We also conducted a worst-case analysis. Secondary outcomes included pain intensity and relief, quality-of-life questionnaires (kinesiophobia, pain catastrophising, functional impairment, fatigue, sleepiness, anxiety and depression), and drugs and non-drug therapy use, compliance to spa therapy and therapeutic patient intervention. We analysed quality-of-life scores through univariate and multivariate analysis of variance.

#### Results

In 2015-2016, 164 patients were recruited, 157 were eligible and randomised to SST arm (78) and SST+TPE arm (79). They were mostly women (95 %), between 40 to 60 years (73 %), and 22 % suffered from severe or morbid obesity. The mean FIQ score was 60/100 points (standard error (SE) 1), with a mean pain intensity of 7/10 points (SE 0). We observed: 8 patients withdrew consent (SST: 5 (6 %) vs SST+TPE: 3 (4 %)); 6 were lost to follow-up (3 (4 %) in each arm); 29 discontinued the strategy (4 (5 %) vs 25 (32 %), p<10-4) for painful episode (3 vs 2), adverse event (0 vs 3) and patient's choice (1 vs 20). Notably, and contrary to SST+TPE arm, the delivery of strategy in SST arm ended at D18, so that, by nature, no discontinuation could happen afterwards.

Spa therapy was effective at D18 (-12/100 points on FIQ, -2/10 points on pain intensity, -4/32 points on fatigue), with continuing efficacy until the end of follow-up.

Altogether, 15 (10 %) FIQ values were missing at M06 (10 (13 %) vs 5 (6 %), p=0.17). The difference between arms in FIQ mean change at M06 was -6 points: -3 (SE 2) for SST vs -9 (SE 2) for SST+TPE (p=0.053) in the primary analysis. The worst-case analysis was inconclusive: p=0.96 and p=0.004.



**Figure.** FIQ mean change according to missing values imputation method. SST (solid line) vs SST+TPE (dashed line).

We found no overall effect of strategy on quality-of-life scores at M06 in a multivariate analysis of variance (p=0.32), but a small benefit in pain relief (+3.2 vs +4.3, p=0.03) and fatigue (-1.6 vs -3.7, p=0.02). Arms did not differ in drugs (p=0.20) or non-drug therapy (p=0.48) evolution. However, 84 % patients in SST+TPE arm declared continuing the recommended physical exercises at M06.

#### Conclusion

A limited effect of therapeutic patient education added to spa therapy was observed on fibromyalgia impact and pain, though not large enough to reach statistical significance. This may result from a level of information on fibromyalgia and its management higher than expected in our population. Nevertheless, the mid-term compliance to recommended physical exercises was high.

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# EFFECTIVENESS OF REHABILITATION TREATMENTS IN THE ITALIAN THERMAL ENVIRONMENT ON PATIENTS SUFFERING FROM MUSCULOSKELETAL DISORDERS: A MULTICENTER STUDY

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Keywords: spa therapy; mud; peloidotherapy; thermal water; rehabilitation

#### Introduction

In Italy, there are numerous thermal structures exploiting waters and muds with specific physicochemical characteristics for treatment, prevention and rehabilitation of several diseases. This multicentre observational study aims to investigate the impact of rehabilitation treatments conducted in the spa setting in patients suffering from subacute and chronic/degenerative musculoskeletal diseases.

#### Methods

Through the involvement of six spas located throughout the country, 151 patients have been enrolled (104 females and 47 males with an average age of 64,55 years). To them a questionnaire designed to mainly assess pain and Quality of Life (QoL) before rehabilitation and after the treatment has been given. Evaluation scales considered in the questionnaire were Numerical Rating Scale (NRS), Short Form Health Survey (SF-12), and EuroQol-5D (EQ-5D), administered in the Italian validated version.

#### Results

Data analysis has highlighted that rehabilitation carried out in the spa environment leads to a statistically significant improvement in pain perception and QoL: on average NRSp improves by 2.50, SF-12 Physical Component Summary (PCS) by 4.22, SF-12 Mental Component Summary (MCS) of 7.03, and EQ-5D of 0.25.

#### Conclusion

This study seems to suggest an important role of rehabilitation treatments in the spa setting on pain and QoL of musculoskeletal disorders patients. Further studies are desirable in order to evaluate in real life the medium and long-term benefits of rehabilitation treatment conducted in the spa environment.

## EFFECTS OF BALNEARY TREATMENTS FROM TECHIRGHIOL AREA ON FUNCTIONING OF PATIENTS WITH DEGENERATIVE LOW BACK PAIN

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Keywords: chronic degenerative lumbar pain, balneotherapy, peloidotherapy, rehabilitation treatment, Techirghiol

#### Introduction

Low back pain is a common health problem that affects people of all ages, and its consequences are considered to have trivial importance. Low back pain affects the quality of life but affects also the patient's performance because the mobility of the lumbar spine decreases, having a negative impact on patients. The prevalence of this condition is about 84 % throughout life and is increasing with age. Degenerative pathology of the lumbar spine is a common cause of low back pain, it is associated with a variety of symptoms due to the variety of anatomical structures at this level that can be affected and can cause pain. Patients with this pathology benefit from multiples treatments, but rehabilitation treatments have a long-term effect, which helps to increase mobility and improving their quality of life.

#### Methods

This study evaluates 130 patients with chronic degenerative lumbar pain, admitted to Balneal and Rehabilitation Sanatorium of Techirghiol, for a period of 2 weeks during the summertime, who were divided into 3 groups: a group performed peloidotherapy with hot mud baths, a group performed peloidotherapy with cold mud baths, and the third group without peloidotherapy, but all patients underwent electrotherapy, massage, and kinesiotherapy. Patients were evaluated using Back Performance Scale (BPS) before and after treatment. This scale analyzes the patient's mobility.

#### Results

Statistical analysis of the scale revealed that the groups of patients with balneary treatments had significant improvements of mobility after rehabilitation treatment (p<0.05).

#### **Conclusions**

We can conclude that complex rehabilitation treatments using natural therapeutic factors increase mobility of the patient with chronic degenerative low back pain, with the big improvement of the functioning and the quality of life.

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### CRENOBALNEOTHERAPY FOR LOW BACK PAIN, SYSTEMATIC REVIEW OF CLINICAL TRIAL

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Key words: Low back pain, Crenobalneotherapy, Balneotherapy, SPA therapy, Hydrotherapy, Water exercise

Prospero database registration

#### Introduction

Crenobalneotherapy is a treatment commonly used in Europe and Middle East. It uses mineral water sometimes combined with different hydrotherapy techniques. Most patients treated in spa centers suffer from low back pain. The purpose of this work is to identify clinical trials on crenobalneotherapy for low back pain.

#### Method

Publication research was performed on Medline, Cochrane, and Pedro databases. Clinical trials were analyzed for internal validity, external validity, quality of statistical analysis and quality of collection of adverse events. We present the best level of evidence

#### Result

Bibliographic research identified 21 clinical trials and the coauthors added 5 references. The 26 trials represent 2695 patients. Some have good methodological quality and allow considering crenobalneotherapy as a potential treatment for low back pain, even if the role of mineral water remains uncertain. The methodological quality of therapeutic trials should be improved. These trials should be analyzed in the future guidelines on low back pain.

## BALNEOTHERAPY FOR CHRONIC SHOULDER PAIN – DATA OF EVIDENCE

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Balneotherapy or spa therapy are usual treatments for patients with chronic shoulder pain but poorly and recently, investigated. Literature investigation identifies four randomized controlled trials publish in peer-reviewed english speaking journals with impact factor [1-4].

3 out of 4 [1,3,4] assess the addition of bathing in natural mineral water (NMW) to a physiotherapy program (mainly based on physiotherapy and exercise), 1 compared spa therapy to usual care [2].

The patients treated complained with chronic shoulder pain due mainly to chronic tendinitis (long biceps brachii' tendon sheath, supraspinatus, rotators cuff) eventually with some degree of impingement.

The main facies of NMW were tested (sulfide, sulphated, brine, bicarbonate, oligometallic NMW). Individual bathing, muds application, water and land-based exercise programs were the usual components of the different treatments delivered to patients during at least three weeks.

Pain was assessed using VAS [1,3,4] but also by the Dash questionnaire [2,4], Spadi [1,3] and SF36 [1,2,4]. Disability was measured using the Spadi (shoulder pain and disability) [1,3] or the quick Dash (disability arm, shoulder, hand) [2,4]. Quality of life was assessed with the short form 36 (SF 36) [1,2,4] or the Nottingham health profile [3]. The patients were assessed at the end of treatment [3], 2.5 or 3 months [4,1], 6 months [2]. All these trials showed an improvement of pain, disability and physical components of quality of life.

More investigation with more robust RCT is needed.

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# PHLEBOLOGY - NUTRITION CONNECTIVE TISSUE DISEASES - VARIA SPA THERAPY FOR CHRONIC VENOUS INSUFFICIENCY: DATA OF EVIDENCE

**Patrick Carpentier - Lecture** 

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Keywords: Balneotherapy; Venous Insufficiency; Randomized Controlled Trial; Patient Education

#### Introduction

Chronic venous insufficiency (CVI) is a widespread disabling condition, which affects approximately 5 % of the general population in the industrialized countries, and impose a heavy economical burden on the national health systems mainly related to the cost of leg ulcers, their ultimate complication. Main etiologies are primary varicose veins and post-thrombotic syndrome, and in both cases, the insufficency of the calf muscle pump, which is the main factor for the lower limbs venous drainage, is the central pathophysiological mechanism. In the many patients whose CVI cause cannot be cured, compression stockings combined with physical activity and rehabilitation are the standard of care. Balneotherapy, organized as 3-week stay in a dedicated spa resort based mainly on hydrotherapeutic rehabilitation, often reinforced by patient education, was found very efficient in improving the pain, quality of life and physical status of these patients, and this presentation reviews the data presently available on this topic.

#### Methods

A recent Cochrane Collaboration review on this topic [de Moraes Silva MA et al, 2019] selected 7 randomized controlled trials (RCT) investigating this field, but only four of them had at least a three-month follow-up, which is needed for a reliable therapeutic evaluation.

- Mancini et al. [2003] investigated 70 patients with varicose viens associated or not with CVI, who were randomized in two parallel groups, one of 20 subjects treated by elastic stockings, and 50 with the same elastic compression and an addicitional active balnetherapeutic program during two weeks (12 days) in a sigle center. The main outcome criterion was generic quality of life at six months.
- Carpentier et al [2009] randomized 59 patients with CVI (CEAP C4 or C5 classes) who underwent a immediately after randomization, or one year later in the control group, a balneotherapeutic course of 4 cares per day during three weeks (18 days) associated with patient education in a single center, and measured the influence of the treatment on the level of skin pigmentation at the ankle level (a surrogate for CVI skin damage) as main outcome criterion, pain (VAS), and CVI related quality of life (CIVIQ2 scale) at 3, 6, 9 and 12 months.
- Carpentier et al [2014] randomized 425 patients in a multicenter trial involving all 12 French spa resorts dedicated to the treatment of venous diseases. A similar treatment of 4 balneotherapeutic care sessions per day during 18 days was provided to the patients of both groups, immediately after randomization in the treated group, and one year later in the control group. Main outcome critrion was the annual incidence of leg ulcers, and secondary criteria CIVIQ quality of life scale, VAS pain scale and Rutherford CVI clinical score at 6 and 12 months.
- Forestier et al [2014] performed a monocenter RCT in 99 patients with C3 or C4 CVI, who underwent a 3 week balneotherapeutic course with 4 care sessions per day after rnandomization in the treatment group, and 3 months later in the control group. Primary outcome criterion was the improvement of the CIVIQ scale, assessed as the success rate of a 20 % improvement of the scale.

#### Results

All four studies showed a substantial and significant improvement of quality of life in those CVI patients, and the Cochrane meta-analysis confirmed a significant improvement of

- CIVIQ2 scale at 3, 6 and 12 months,
- EQ5D generic quality of life scale at 6 and 12 months,
- VAS pain scales at 3, 6 and 12 months,
- and cutaneous pigmentation at 12 months.

#### Conclusion

These work demonstrate the high therapeutic potential of balneotherapeutic programs in patients with chronic venous insufficiency. The impact of the hydrotherapeutic rehabilitation on the calf muscle pump is probably the main mechanism of this impact, but remains to be scientifically investigated. A synergistic effect of therapeutic education programs developed in some spa resorts could also account for some positive influence. Further optimization of the present balneotherapeutic programs is certainly possible.

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# IMPACT OF A 12-MONTH WEB AND SMARTPHONE-BASED INTERVENTION INITIATED DURING SPA THERAPY TO IMPROVE LONGTERM PHYSICAL ACTIVITY OF PATIENTS WITH CHRONIC DISEASES: RANDOMIZED CONTROLLED TRIAL

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#### Background

Lack of physical activity (PA) and sedentary behaviors are leading risk factors for non-communicable diseases (NCD). Web-based interventions are effective in increasing PA in older adults and in NCD patients. In many countries a course of spa therapy is commonly prescribed to NCD patients and represents an ideal context to initiating lifestyle changes.

#### **Objective**

The main objective of this study was to evaluate in NCD patients the effectiveness of an intervention combining an individual face-to-face coaching during spa therapy and, when returning home, a web- and smartphone-based PA program including a connected wrist pedometer and a connected weighing scale, on the achievement of physical activity guidelines (PAG) 12 months after the end of spa therapy.

#### Methods

This was a 12-month, prospective, parallel-group, randomized controlled trial. Patients were enrolled during spa therapy and randomized 1:1 to intervention or control group who received usual advices about PA. From the end of spa therapy, PA, weight, waist circumference, and quality of life of the participants in both groups, were assessed by phone every 2 months. Primary outcome was meeting PAG (PA≥600 METs) at 12 months after the end of spa therapy. Secondary outcomes were: meeting current PAG at 6 months of follow-up; sedentary time, weight and waist circumference, PA and quality of life, at 6 and 12 months. Objective use data of the web-and smartphone-based PA program were collected. Analytic methods include intention-to-treat and constrained longitudinal data analyses.

#### Results

The study sample was 228 patients (women: 77.2 % (176/228), mean age: 62.4 years (SD 6.7), retired: 53.9 % (123/228), mean BMI = 28.2 kg.m-2 (SD 4.2)). No group differences were found for any baseline variable. At 12 months, the proportion of patients achieving PAG was significantly higher in intervention group versus control group (81 % vs 67 % respectively, OR = 2.34 (95% CI 1.02- 5.38; *P*=.045). No difference between intervention and control group was found neither in achieving PAG at 6 months nor for sedentary time, weight and waist circumference, at 6 and 12 months. Regarding quality of life, the physical component subscale score was significantly higher at 12 months in intervention group versus control group (mean difference: 4.1 (95% CI 1.9-6.3; *P*<.001). The mean duration use of the program was 7.1 months (SD 4.5). Attrition rate during the first 2 months of the program was 20.4 % (23/113) whereas 39.8 % (45/113) of the participants used the program for at least 10 months.

#### Conclusions

The results showed significantly more participants meeting PAG at one year in the intervention group compared to controls. A course of spa therapy offers the ideal time and setting to implement education in PA. Digital coaching seems to be more efficient than usual coaching for increasing the level of PA and decreasing sedentariness on the long term.

#### Trial Registration:

ClinicalTrials.gov NCT02694796; https://clinicaltrials.gov/ct2/show/NCT02694796. Funding: Afreth (Paris, France)

# LONG TERM EFFECT OF SPA THERAPY COMBINED WITH PATIENT EDUCATION PROGRAM ON SUBJECTS WITH OVERWEIGHT AND OBESITY – A CONTROLLED STUDY

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#### Introduction

The aim of this single center prospective controlled study in volunteers with obesity and overweight was to evaluate the effect of a patient therapeutic education program (PTE group) combined with spa therapy on weight, physical activity, eating habits and quality of life versus spa therapy alone (control group).

#### Methods

The PTE group of 151 subjects with obesity or overweight followed a 3-week program combining patient education with spa therapy and 189 attended a course of spa therapy alone. The main endpoint was weight change at 5 months after the end of the program.

#### Results

At 5 months significant loss was observed in the PTE group compared to controls (-2.69 kg vs -1.24 kg, p=0.008), a relative weight loss of -2.8 % vs -1.3 %. At 11 months after spa therapy, only the PTE group maintained a weight loss in addition to the weight loss obtained during spa therapy. The control group returned to the weight they had at the end of spa therapy. In both groups, a significant increase in physical activity was observed at 5 (p<0.001) and 11 months (p<0.001) with a significant better improvement in the PTE group. In addition, while in both groups some quality of life parameters and dietary choices were improved, the improvement (more fruit, vegetables, fish and water) was significantly higher in the PTE group, at both 5 and 11 months after spa therapy.

#### Conclusion

In conclusion, while spa therapy alone initiated positive changes in weight loss, physical activity and some Quality-of-life parameters, the PTE program enhanced this effect.

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Funding: Afreth (Paris, France)

## THERMAL DISPARITY AMONG FINGERS AND ITS AMELIORATION BY CO<sub>2</sub>-WATER BATHING IN CONNECTIVE TISSUE DISEASE PATIENTS

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Keywords: carbon dioxide; thermography; thermal disparity; peripheral circulation; connective tissue disease

#### Introduction

Peripheral vascular disorder including Raynaud's phenomenon is one of the major features associated with connective tissue diseases (CTDs), in that, thermal disparity among fingers has been reported. Meanwhile, CO<sub>2</sub> has long been known to improve peripheral circulation. Whether the thermal disparity may be ameliorated by CO<sub>2</sub> is a major concern.

#### Methods

CTD patients with suspected peripheral circulation disorder underwent a thermography test. From before to 30 min after hands immersion in CO<sub>2</sub>-water (1000 ppm CO<sub>2</sub>, 42°C,

10 min) or tap-water (42°C, 10 min; Tap), the nailfold temperatures were followed. The mean temperature (m-Temp) and the coefficient of variation of the temperature (CV=SD/m-Temp of one hand; the mean of CVs of both hands was adopted as the indicator of thermal disparity) were monitored.

#### Results

Forty-seven (45 women/2 men) patients were included for  $CO_2$  bathing, and 52 (49/3) were for Tap bathing. As for  $CO_2$  bathing, the m-Temp was  $30.8 \pm 3.0^{\circ}$ C at the baseline,  $35.3 \pm 1.0^{\circ}$ C immediately after, and  $32.1 \pm 1.9^{\circ}$ C 30 min after. CV was  $0.0291 \pm 0.0247$ ,  $0.0135 \pm 0.0039$  and  $0.0163 \pm 0.0143$ , respectively, and remained significantly lower than the baseline throughout until 30 min after. No significant re-increase of CV from that just after  $CO_2$ -bathing was observed. As for Tap bathing, the m-Temp was  $31.5 \pm 2.9^{\circ}$ C,  $36.4 \pm 0.7^{\circ}$ C, and  $32.5 \pm 2.0^{\circ}$ C; CV was  $0.0236 \pm 0.0200$ ,  $0.0102 \pm 0.0036$ , and  $0.0181 \pm 0.0150$ . CV after Tap bathing was lower than that at baseline till 30 min after, but when comparing CVs to the CV just after Tap bathing, CV re-increased at 15' after and later.

#### Conclusion

Thermal disparity among fingers was observed at baseline measurement in CTD patients. Warm CO<sub>2</sub> bathing markedly ameliorated the disparity; this amelioration remained until after 30 min. Whereas, the amelioration after Tap bathing tended to reverse earlier.

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#### Figure

Mean CV change from before to after CO<sub>2</sub>-water and Tap-water bathing. CV decrease was maintained till 30' after CO<sub>2</sub> bathing, while CV re-increased from 15' after Tap bathing.

## LAY PERSPECTIVES OF QUALITY OF LIFE IN RHEUMATOID ARTHRITIS PATIENTS: THE RELEVANCE OF PSYCHOLOGICAL DISTRESS

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Keywords: Quality of Life; Rheumatoid arthritis; ICF; WHOQoL; HAQ-DI

#### Introduction

In Portugal, epidemiological data on rheumatoid arthritis (RA) patients demonstrated bigger disability and worse quality of life within rheumatic diseases. Moreover RA has a variable course, often with periods of exacerbations and, less frequently, true remissions. Quality of life (QoL) in RA patients has been focus of great interest over the last years, but often lacking the way QoL is defined by patient's own words.

The aim of this study is to increase the understanding of Quality of Life (QoL) in RA patients under spa treatment protocol and explore the personal features of living with the disease, namely autonomy within the World Health Organization Quality Of Life (WHOQoL) framework.

#### Methods

Use of a semi-structured questionnaire which assess socio-demographics variables, functional status and patients' health status with Stanford Health Assessment Questionnaire Disability Index (HAQ-DI). Then, three open questions were made targeting the patients' difficulties and worries in having RA.

Descriptive statistics were made for sociodemographic information and health status. Qualitative data was transcribed, analysed and coded within the WHOQoL and ICF (International Classification of Functioning).

#### Results

Sixty-two RA patients (MAge = 56.7; SD = 11.2; women = 83.9 %) were interviewed. Most patients lived with RA for a long period of time (M = 16.5 years; SD = 11.6) and presented moderate HAQ-DI scores (M = 1.37; SD = 0.75). Main features of QoL in RA highlight the importance given to physical health, particularly to independence and autonomy.

#### Conclusion

Main results reinforce the weight of feeling independent and autonomous, and support that along with RA's physical symptoms and associated functional limitations, psychological aspects are of great value to these patients' QoL, namely in spa treatment.

## PHYSICAL FUNCTIONING QUESTIONNAIRE FOR AUTOIMMUNE DISEASES PATIENTS.

#### PRELIMINARY VALIDITY, RELIABILITY AND SENSITIVITY STUDY

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Keywords: Autoimmune diseases; Functioning questionnaire; Patient expert; Hydrology

#### Background

Patients' physical functioning in autoimmune diseases is a core issue not only for clinical decisions concerning treatment, but also to the assessment of the effectiveness of those treatments.

However, a comprehensive physical functioning assessment requires a methodical and careful inquiry, which is difficult in most clinical practices.

Several self-administered questionnaires have been developed as a useful alternative but many of them aim just to collect data for screening or research, being limited in their scope. Patient's participation must be emphasized in studies protocols.

#### **Objectives**

To present the Physical Functioning Questionnaire for Autoimmune Diseases Patients, enhancing hydrology treatment and based on patients' opinion.

#### **Questionnaire**

Physical Functioning Questionnaire for Autoimmune Diseases Patients is standardized, self-administered questionnaire, designed to provide information about patients' physical functioning.

#### **Procedure**

An item swimming pool was constructed based on: literature review, analysis of several physical functioning and functional status questionnaires.

Through expert's opinion (patient and health professional), there were selected 54 items, which were incorporated into the final version of the questionnaire.

Patients answered to the questionnaire.

#### **Participants**

- N = 90 patients
- Diagnosed with autoimmune diseases
  - 37.9 % rheumatoid arthritis
  - 12.6% psoriatic arthritis
  - 14.9 % ankylosing spondylitis
  - 23 % lupus

- 1.1 % inflammatory myopathies
- 10.3 % scleroderma
- Disease duration between 1 and 27 years (M=10.55; SD=7.11)
- 77.8 % women
- Aged between 22 and 74 years (M=49.96; SD=13.62)

#### Discussion/Conclusion

Patient's wishes and difficulties must be considered, particularly in terms of functionality. As a result, better acceptance of the prescribed therapy is achieved. In addition to an improvement in activity and autonomy, besides this quantification of outcomes we hope to provide better quality of life of these disabling diseases.

We believe that the results of this preliminary study are encouraging, suggesting that this is a valid, reliable and sensitive questionnaire.

However, it will be important to continue the study of this questionnaire with a larger number of patients not only to allow us to test their sensitivity to specific autoimmune diseases but also to include these patients much more for the construction of the questionnaire in future balneology clinical research.

#### NERVOUS SYSTEM DISORDERS

## WATER BASED THERAPY IN CHRONIC NEUROLOGICAL CONDITIONS : A SWIM THROUGH SOME PARTICULAR METHODS

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Keywords: Aquatic therapy, Bad Ragaz, Watsu, Halliwick, Ai Chi

#### **Abstract**

Hydrotherapy uses the physical properties of water as a mean to promote patient rehabilitation in many pathological conditions. Many specific methods have been used in clinical practice. Among the most studied are the Bad Ragaz Ring Method (BRRM), the Halliwick concept, Watsu and Ai-Chi. This work will review some technical aspects of these methods, with a particular focus on neurological conditions.

#### Methods

A bibliographic search using electronic databases was conducted, including PubMed, PEDro and Google Scholar. Articles were selected if they discussed the practice of specific protocols from the aforementioned water therapy methods. Articles were further scrutinized for their application on specific neurological conditions.

#### Results

The search results retrieved 67 articles regarding the use of these programs for treatment of specific conditions (both neurological and non-neurological).

After exclusion of duplicates and non-relevant studies, a total 44 were included for review (Watsu 14 studies with 3 RCT; Halliwick 10 studies with 4 RCT; Bad Ragaz 6 studies with 3RCT; Ai Chi 13 studies with 12 RCT; Ai Chi + Halliwick 1 study – 1 RCT). Therefore, on the total, 23 were Randomized Controlled Trials (RCT), 6 were Non-Randomized Controlled Trials (NRCT) and 15 were Case Reports (CR) and small Case Series (CS). The most common neurological clinical conditions where water therapy methods were used were: Stroke, Cerebral Palsy and Parkinson Disease.

Most of these studies described poorly the components and details of the several programs. The BRRM uses different water movement patterns and proprioceptive neuromuscular facilitation principles to improve patient's functional disabilities. This technique is complex and requires significant therapist training to learn the various movement patterns. The method includes isometric, isotonic and isokinetic contractions, structured in movements of the torso, arms and legs that can be unilateral or bilateral, symmetrical or asymmetrical. Regarding neurological conditions, there is only one available trial in stroke patients which has shown significant positive effects.

The Halliwick concept teaches patients with disabilities to participate in water activities. These activities become progressively more difficult and with lesser therapist assistance. This method uses a 10-point program, in which there is a process of development through phases which include mental adjustment, balance control, and movement patterns until independent water movement is achieved. Various studies concerning the Halliwick concept have been done in various neurologic conditions such as stroke, cerebral palsy, Parkinson disease and Multiple Sclerosis with significant benefits for the patients.

Watsu is the application of Zen Shiatsu principles to persons floating in water. It combines cradles, gentle stretching, massage and structured movement sequences performed at surface level. The Watsu method can facilitate relaxation, pain decrease, improvement of muscle tone and reduce spasms. Many of these aspects could be of benefit in many neurological diseases, however the application of this method has been the least studied for this indication, with no randomized trials ever performed.

Ai-Chi places emphasis on balance training. Based on the land counterpart it consists of 16 movements (named katas), including breathing, upper and lower limbs, trunk balance and coordinated movements. The sequence is performed in a slow and controlled manner. By allowing the performance of balance training in a safe water environment, this method can be useful in diseases where balance problems cause significant disability as is usually the case of many neurologic diseases, in which this method has been frequently studied.

#### **Conclusions**

Water therapy methods have potential to become an important step towards rehabilitation of various medical conditions. The application of these techniques is complex in execution, requires knowledge of the physical properties of water and significant training from the personnel involved. Thus it could be useful to provide a more detailed and clearer description of the used techniques in the research studies. Nonetheless the available literature on the subject has been encouraging with many studies showing significant positive benefits in a multitude of pathological conditions.

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## THE ROLE OF AQUATIC THERAPY IN CEREBRAL PALSY: IS WATER-BASED THERAPY BETTER THAN LAND?

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Email of presenting author: saracaldasafonso@gmail.com Keywords: Aquatic therapy; Cerebral Palsy; Rehabilitation

#### Introduction

Cerebral palsy (CP), the most common motor disability in childhood, is defined as a range of disorders of motor and postural development which causes lifelong functional limitations. This are attributed to a non-progressive disorder that occurs in fetal development or child's brain. Although the brain lesions that result in cerebral palsy are not progressive, the clinical symptoms of CP may change with time as the individuals grow and develop. Majority of children with CP suffer from the spastic form with a minority of cases being primarily dyskinetic, ataxic or hypotonic. Concerning aquatic therapy, the aquatic environment has broad rehabilitative potential, extending from the treatment of acute injuries through health maintenance in chronic diseases. Particularly in CP, aquatic therapy has gained popularity among physicians due to its mechanical and thermal effects. The aim of this paper is to review recently published literature since 2000 with a focus on aquatic exercise for children with CP and analyze if it could be consider one of the best treatment options.

#### Methods

A literature review was conducted using electronic databases. This included, Medline (via PubMed), ISI Web of Science and Google Scholar, from de the year 2000 to the current date. We used the following keywords: Aquatic therapy, cerebral palsy and

rehabilitation. Terms were combined using Boolean operators. We furtherer our research by accessing the selected articles bibliographic references for inclusion of any potential missing articles. Inclusion criteria were population (children and adolescents with CP), intervention (aquatic: aerobic, anaerobic, strength, and other), and outcome (body function, activity, and participation).

#### Results

Using the methods described, 26 articles were retrieved in the initial search, from which 6 articles were selected on the basis of applicability, relevance and exclusion of duplicates. Two systematic reviews analyzed a total of nine aquatic exercise studies involving children and adolescents with CP, specially spastic CP with varying levels of gross motor function classification system (GMFCS). All reported positive effects in flexibility, muscle strength, gait, and gross motor function scores and mobility performance at home, and community environments. A quasi-experimental study of 24 participants demonstrated that the aquatic therapy group improved more than the control group for children at GMFCS level II and for children with the spastic diplegic subtype. Moreover, the change in 66-item Gross Motor Function Measure scores and physical activity enjoyment scale was greater in the pediatric aquatic therapy group than the control group, even for children with GMFSC level IV. However, the beneficial effects on pediatric aquatic therapy on motor function did not translate into improvements in activities of daily living and health-related quality of life. A clinical study with 32 patients, comparing land vs aquatic exercises for children with spastic CP reported that aquatic exercises are as effective as land-based exercises for spasticity management and motor function improvement in children with CP. However, aquatic exercise can result in a higher level of improvement in quality of life scores than the landbased exercises. A study, with 10 participants, compared the use of the Halliwick Concept vs normal activities and reported that the aquatic programme-based group showed increased motor function following the intervention, compared to the control group. Furthermore, the aquatic-based therapy improved the average score for gross motor function measurement, post-intervention. Finally, a study including 30 patients, compared a 10week aquatic exercise training experimental program on gross motor function in children with spastic CP vs the same program on land. This study reported that only the experimental group showed significant improvement in all dimensions of gross motor function except for walking, running, and jumping. Statistically significant difference was found between both groups for all dimensions of gross motor function after 10 weeks of intervention.

#### Conclusion

These findings suggest that there is a strong potential for aquatic physical activity to benefit children and adolescents with CP, especially if they have a GMFSC IV-V and are very limited to perform land-based therapies. Majority of the studies concluded that aquatic therapy enhances motor function and enjoyment for children with cerebral palsy.

Multiple studies concluded that aquatic therapy had shown better results in gross motor function comparing to land-based therapy and that aquatic therapy should be a part of the regular therapy program. However, future studies should involve participants across the GMFCS spectrum, include larger sample sizes, longer follow-up periods and clear dosing parameters, in order to extrapolate these results to all the patients with CP, despite of their impairments.

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## EVALUATION OF THE FEASIBILITY OF A TWO-WEEK COURSE OF AQUATIC THERAPY AND THALASSOTHERAPY IN A MILD POST-STROKE POPULATION

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Keywords: aquatic therapy; thalassotherapy; stroke; balance; gait; pain; quality of life

#### Introduction

Strokes are a leading cause of disability in developed countries. Patients with disabilities need rehabilitation to improve their physical functioning, mental status, and quality of life. Currently, no high-quality evidence can be found attesting the benefits of any of the interventions that are nowadays used. Water-based exercise may improve the physical conditions and quality of life for people in the post-stroke phase. The objective of this study is to test whether aquatic therapy in an enriched environment at the sea side (a thalassotherapy centre), could play a role in this condition.

#### Methods

A quasi-experimental prospective study consisting of a specific programme assessed 62 patients with a mild-moderate disability pre- and post- 2 weeks of intensive treatment. They followed a thalassotherapy regimen including aquatic therapy in a sea water pool at 32-34 degrees C for 45 min daily 5 times a week. The outcomes measured were the: Berg Balance scale, Timed Up and Go test, 10-metre walking test, 6-minute walking test, Pain Visual Analogue Scale, WHO Well-being index, EuroQoL VAS and EuroQoL 5D.

#### Results

We observed a significant improvement in all outcomes measured (p<0.001, except mobility EuroQoL p<0.05), except in the other four dimensions of the EuroQoL 5D and 10-metre walking test (NS).

#### Conclusion

A two-week intensive course of aquatic therapy and thalassotherapy may be beneficial in the short-term by reducing pain and improving the functional status and overall well-being in post-stroke patients.

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### THERMAL BATHS IN PARKINSON'S DISEASE: A PLAN TO PROMOTE QUALITY OF LIFE

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#### Background

Parkinson disease a chronic condition with a significant impact from the functionality and quality of life point of view. Gait, postural instability, stiffness, breathing dynamics and pain are the main areas affected in these patients [Alves Da Rocha, McClelland, & Morris, 2015; Campos, Páscoa Pinheiro, Branco, & Figueiredo, 2009; Carroll, Volpe, Morris, Saunders, & Clifford, 2017; Volpe, Giantin, Maestri, & Frazzitta, 2014].

#### **Objectives**

Creation and monitoring of a specific rehabilitation plan for patients with Parkinson disease, promoting synergism between the thermal water properties, the most current neurological rehabilitation techniques and an involving and relaxing landscape, in order to obtain gains in the physical and cognitive capacities and in the well-being of these patients.

#### Methods

Implementation of a personalized plan by a Physiatrist and accompanied by a Physiotherapist, lasting 12 days and divided into 2 parts throughout the day. Training in

the context of a thermal pool and training in a gym. At weekends, the patient integrates specific classes of cognitive stimulation and relaxation. Completion of a final satisfaction questionnaire.

#### Results

Over the 9 months of implementation, 9 patients entered the program, with an average age of  $70 \pm 6.53$  years, of whom 6 were male. 88.9 % of patients agree that the goals set by them and the doctor have been achieved. 100 % of patients agreed that their physical well-being, as well as their psychological well-being improved. 88.9 % felt an improvement in freedom of movement, balance and gait pattern; 85.7 % reported pain improvement. All patients experienced a subjective improvement in their health status and would recommend this program to others.

#### **Conclusions**

In the patient's view, the objectives proposed for this short rehabilitation program were achieved, translating into significant improvements in terms of pain, mobility and quality of life. In the future, more studies will be necessary to carry out with a larger number of patients and with the introduction of more objective physical and psychological measurable variables.

# WATER BASED THERAPY FOR NEUROLOGICAL CONDITIONS : A SWIM THROUGH THE EVIDENCE

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Keywords: Aquatic therapy, Bad Ragaz, Watsu, Halliwick, Ai Chi

#### Introduction

Many concepts of water based therapy have been used over the years in the field of rehabilitation to improve various disease symptoms and patient impairments. The most currently used techniques are the Bad Ragaz Ring Method, the Halliwick concept, Watsu (or Water Shiatsu) and Ai Chi. However to the best of our knowledge no previous work has presented the quality of the available evidence in a comprehensive way to support the use of these methods, particularly in various neurological conditions.

#### Methods

A search of electronic databases was conducted, including PubMed, PEDro and Google Scholar from the year 2000 to the current date with the keywords: aquatic therapy, hydrotherapy, Bad Ragaz, Halliwick, Ai chi and Watsu. Terms were combined using Boolean operators. Titles and abstracts were assessed for relevance to the question being studied. Articles references were further checked for inclusion of any potential missing articles. Among these articles we selected those related to neurological conditions.

Results are presented in a table format. Risk of bias of each study was assessed using the Cochrane risk-of-bias tool for randomized trials and the ROBINS-I tool for non-randomized studies

#### Results

The search method retrieved 67 articles. After exclusion of duplicates and non-relevant studies, 26 were related to neurological conditions and thus included for review. Of the included studies 13 were Randomized Controlled Trials, 5 were Non-Randomized Controlled Trials and 8 were Case Reports and small Case Series. Risk of Bias among studies was assessed to be moderate to high, with only 6 studies (24 %) being classified as low risk of bias. The highest level of evidence was found with the application of Bad Ragaz, Halliwick and Ai Chi in Stroke patients showing beneficial outcomes in balance improvement. Other positive results from higher quality studies were the application of the Halliwick concept and Ai Chi in PD. No higher quality studies were found for Watsu therapy, since most studies on neurological conditions were based on case reports and small series. A single RCT investigated the combination of two water therapy methods (Ai Chi and Halliwick) in stroke patients reporting positive outcomes in balance and knee flexor strength, however study quality was only deemed to be moderate.

#### Conclusion

Aquatic therapy methods such as the Bad Ragaz Ring Method, Halliwick, Watsu and Ai Chi have demonstrated beneficial effects when applied in many clinical scenarios and diseases. In the field of Neurology results have been promising with some medium to higher quality studies showing positive outcomes of the treatment. To reach definite conclusions newer RCTs should strive to reduce the potential sources of bias by improving methodological quality and thus the study power.

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# BENZODIAZEPINE WITHDRAWAL DURING BALNEOTHERAPY FOR STRESS RELATED DISORDERS

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The WHO now considers mental illnesses to be the third leading cause of disease worldwide and predicts a strong increase in these conditions by 2030. They should then become the 1st cause of universal disease. It cannot be denied that modern life is the source of a significant development of stress due to the acceleration of information processes and their dissemination. Today, an essential activity in general medicine and outpatient psychiatry concerns the follow-up of people who suffer from anxiety, sleep disorders, chronic fatigue, or psychosomatic affections such as chronic pain, for which the usual therapeutics often show their limits and also lead to overconsumption of medication, whether in quantity or duration. In recent years, thermal medicine in the field of psychiatry and mental health has demonstrated an indisputable effectiveness as in the Stop Tag study [1]. One consequence of anxiety-related pathologies is the overconsumption of medication. This is a major public health issue. The prevalence of benzodiazepine consumption in France is approximately 15 % over one year, and nearly 10 % of the French population regularly uses these drugs. In order to provide a therapeutic response to this public health problem, a group of academics has set up a psycho-educational protocol for benzodiazepine withdrawal associated with a 3-week spa treatment. Thus, the combination of a spa treatment (as a replacement therapy), medical follow-up and a psycho-educational programme for groups of patients motivated to withdraw was set up. The Specth [2] study consisted in following these patients for a period of 6 months after the spa treatment. This protocol was tested during cures carried out in French psychiatric spas. A total of 70 chronic overconsumers were included in this programme. The evaluation at the end of the spa treatment lasted 6 months. We present here the therapeutic programme set up, the modalities of inclusion in the protocol and the therapeutic results obtained at the end of the 6 months of epidemiological follow-up. The programme of this study, named Specth, allowed a cessation of the consumption of anxiolytics over a period of 6 months for 41 % of the patients, and a reduction of at least 50 % of the initial consumption, for 80 % of these patients. Finally, we provide some information on the continuation of this programme within the framework of the École Thermale du Stress set up in Saujon since 2012, and which has enabled 163 additional patients to be monitored, the results of which will be presented.

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# TRAINING and EDUCATION DOCTORS' TRAINING IN BALNEOLOGY NEEDS AND EXPECTATIONS

# SPECIALIZED TRAINING IN SPA MEDICINE NEEDS AND ISSUES

#### Professor Christian Hérisson - Professor Gisèle Kanny College of Teachers in Spa Medicine

The training offered to future spa physicians has to meet the current challenges and needs of spa medicine, namely:

- To train a sufficient number of spa doctors, that is to say to meet quantitative needs,
- Train spa doctors by taking into account the evolution of the place of spa medicine in therapeutics, that is to say to meet qualitative needs.

#### The auantitative needs

It is today from 700 to 800 physicians who exercise in French spas, some of them full-time and others part-time.

It can be assumed that more than half of current physicians will be retired in the next 5 years. Under these conditions the theoretical training needs are at least 60 to 70 doctors per year. The number of doctors trained today still remains significantly insufficient. There are many reasons for this:

- Overall decrease in the number of medical students.
- Lack of awareness during the 2<sup>nd</sup> and 3<sup>rd</sup> cycle of medical studies.
- Very significant decrease of the university training offer. When the Capacity was established in 1988, it was provided by 7 faculties of Medicine, namely: Clermont 1, Grenoble 1, Nancy 1, Bordeaux 2, Toulouse 3, Montpellier 1 and Marseille 2. Today, the offer is limited to 4 faculties, namely: Grenoble, Nancy, Toulouse and Montpellier.
- Many spa doctors practice in the framework of a late professional reorientation, hence short careers to be considered

Moreover, the health crisis Covid-19 has only worsened the situation leading some practitioners at the end of their career to stop their activity prematurely, but it has also dissuaded young practitioners to engage in this professional way.

#### *The qualitative needs*

Namely the need to adapt to the evolution of spa medicine and to take into account the following elements:

- The fact that spa therapeutics, which had been for a long time centered around the "natural mineral water medicine" is now largely reoriented towards the «crenorehabilitation», that is, spa medicine as a "global therapeutic".
- The undeniable predominance of locomotor indications : Rheumatology, Neurology, Phlebology.
- The reality of a geriatric and gerontological dimension more and more important.

 The possibility of accommodating new pathologies such as the prolonged aftermath of Covid-19.

The proposed training must take into account from a qualitative perspective the desired profile of the spa physician in its different dimensions, namely:

- Prescriber of spa treatments: from the initial assessment, the knowledge of general or local indications, the choice of spa techniques or even their realization through Complementary Medical Practices, the monitoring and the adaptation of the cure, the final assessment and finally the necessary and desired link with the family doctor.
- Actor of health promotion actor, the spa doctor must be a health education actor in areas such as physical activity, diet, tobacco, etc. and he must know how to integrate into Therapeutic Education of the Patient.
- Public health observer : in the context of prevention, screening or epidemiological actions
- Involvement in the spa life: the physician is involved in the organisation of the treatments and particulary the coordination of care with the other spa workers; he/she is also involved in the vigilance procedures in the resort.
- In terms of research and evaluation : it can and must participate in clinical or medicoeconomic studies and can be an actor around research protocols.
- Education and training: It is highly desirable that spa physicians get involved with the academics in the context of medical training but also in the training of other health care providers

In practice today, specialized training in Spa Medicine is therefore faced with two obligations:

- To increase the number of trained doctors to meet quantitative needs and to allow the maintenance of the medical dimension of the spas.
- To adapt the content of the training to be in adequacy with the evolution of spa medicine.

#### Qualifying diplomas in France

Two diplomas provide access to training in Spa Medicine:

- The Capacity of Medical Hydrology and Climatology:
  - This specialized training in Spa Medicine, created in 1988, takes place over 2 years. The conditions of registration require to be holder of the doctorate in Medicine. It

includes a theoretical training of 120 hours, to which is added a practical training in spa of 50 half-days.

- This degree is mainly intended for practitioners who want to work in the spa as their main profession.
- The Inter-University Diploma of Medical Practice in Spas :
  - This is an alternative that has been set up by the University of Montpellier, with the faculties of Nancy, Bordeaux, Clermont-Ferrand and Grenoble.
  - This degree is available to interns during their studies. It includes a training course of about 60 hours of theoretical teaching, a 20-hour internship in a spa medicine practice, and participation in visits to spas.

This degree is not intended to replace Capacity, but rather to provide a training

opportunity for other practitioners who want to get involved in spas, namely:

- Physicians exercising an ancillary spa activity,
- Physicians carrying out replacements of spa doctors
- Practitioners having a late reconversion at the end of their career towards spa medicine,
- And young doctors at the end of initial training.

The College of Teachers in Spa Medicine

The need to perpetuate a specific university training for the exercise of Spa Medicine led to the creation of the "College of Teachers in Spa Medicine". This one gathers together teachers of French Spa Medicine: Academics responsible for the teaching of Medical Hydrology and Climatology, teachers of various disciplines concerned by the Spa medicine, but also the referent spa doctors, involved in training and research.

The activities of the College concern in particular the organization of different courses, theoretical or practical, the writing of books, the creation of teaching documents and tools, and participation in the various instances in partnership with the French Society of Spa Medicine.

This College, a true federative structure, has thus created a dynamic and a synergy of actions, responding, at least in part, to the problem of spa medical training.

# PHYSIOTHERAPY AND HYDROTHERMALISM IN BRAZIL: FORMATION OF PHYSIOTHERAPY AT THE FEDERAL UNIVERSITY OF PARANÁ

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Keywords: Physiotherapy, Hydrotherapy, Education, Health Education, Thermalism

#### Introduction

The training of physiotherapists in Brazil follows the National Curricular Guidelines for the Undergraduate Physiotherapy Course (NCGUPC). There is a need for differentiated learning processes, such as project-based learning, with theoretical, practical and field classes to experience the different local realities and Physiotherapy resources. Thus, the perception of the professional future must meet the educational pillars of knowing, doing, living and being a member of the health team, in addition to building as a physiotherapist pedagogical knowledge with experiences of clinical practice. Within the physiotherapist's area of activity, hydrotherapy stands out, which makes use of drinking water in liquid (immersion in a heated pool), solid (cryotherapy) or gaseous (inhalation) states, for several purposes [Israel et al., 2017]. Belonging to this context, we have thermalism that benefits therapeutically from mineral, thermal and mud waters, in a

broad social context, which involves health, administrative, tourist and medicinal issues [Alpoim, 2010; Israel et al., 2017]. In the light of this information, the objective of this study is to report the experience of the discipline Physiotherapy and Hydrothermalism on Brazilian public university.

#### Methods

The Physiotherapy course at the Federal University of Parana (FUP) - Brazil, proposed the inclusion of the discipline Physiotherapy and Hydrothermalism, with active learning processes with practical experiences in thermalism. There are theoretical meetings and a field trip in the south and southeast regions of Brazil.

In 2019 the field trip was the thermal waters of southern Brazil in the cities of Santo Amaro da Imperatriz-Santa Catarina, a place that is considered a historical heritage, has a hydrothermal spring, allowing the experience of balneotherapy using baths, whirlpools, pools and waterfalls [Karagülle; Karagülle, 2015]. Afterwards, spa therapy practices were carried out in the city of Florianopolis-Santa Catarina. The existing therapies are: thalassotherapy, Scottish shower, vicky shower, water circuit and balneotherapy. Thus, there are benefits for the well-being and quality of life of the people who are served there [Lo et al., 2015].

At the end of the aforementioned Physiotherapy and Hydrothermalism discipline, academics worked out in group a final product of their theoretical learning (based on scientific evidence from the field) and practical visits made in a book chapter format, a booklet with physiological benefits of thermal waters and a digital portfolio with images of the spaces visited.

#### Results

Thirty participants, all Physiotherapy students of FUP, had the opportunity to learn and experience in the practice of Physiotherapy and Hydrothermalism for health promotion, counting on the physiological effects on muscle tone and tension, skin, digestive system, pain, relaxation, mobility and body functionality, detoxification and body hydration [Fioravanti et al, 2014]. It was possible to discuss the scarcity of studies in the area, the lack of health professionals in thermal environments, especially physiotherapists who experienced the reality of thermalism and health education, aiming at the benefits achieved by spa and spa users.

FUP allows Physiotherapy students the theoretical and practical knowledge of hydrothermal environments as a physiotherapeutic resource, in addition to providing a comprehensive look with interprofessional contact, diversifying and expanding the area of activity with a playful and attractive learning for future physiotherapists.

#### Conclusion

Thus, through studies and pedagogical practices within the University, with interaction of the teaching, research and extension triad, it is observed that this experience added knowledge and expanded the performance of Aquatic Physiotherapy and

Hydrothermalism in Brazil, but still little explored by physical therapists and health researchers. With that, it is expected that the future physiotherapist can occupy these spaces and deepen the practices in evidence and thus improve health care.

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# TRAINING IN THE INSTITUTE OF THERMALISM OF THE UNIVERSITY OF BORDEAUX

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Keywords: trainings, balneology, health, professional diplomas, bachelor

In France, in the fields of balneology, water and health, besides the specific training provided to doctors to acquire skills related to the practice of thermal medicine, there are other training courses dedicated to the professions of hydrotherapy, well-being, health prevention, technical management of health risk, administrative management.

Created in 2000 by decree of the Ministry of Higher Education and Research, the Institute of Thermalism of the University of Bordeaux plays a major role in those training courses. Located in Dax, on the territory of Les Landes, one major balneology territory in France, the Institute of Thermalism offers a very diverse range of training

courses integrated into the European License-Master-Doctorate (LMD) system or Bachelor-Master-Doctorate system, accessible to continuing vocational training, lifelong learning. The Institute of Thermalism offers professional diplomas leading to various jobs: spa manager, assistant spa manager, thermal technician, technical manager, hydrotherapist, health prevention supervisors in nutrition and food. The Institute of Thermalism also offers a certification in therapeutic patient education and welcomes first-year students preparing a health degree in medicine, maieutics, odontology and pharmacy with the possibility of accessing a balneology teaching unit.

For two decades, the Institute of Thermalism has been structuring and developping its training offer, based on the needs and skills required by employers. It has trained nearly 1,000 students with a high professional integration rate of 80 % in the field of water and health.

Labelled "Health Campus" in 2018, the Institute of Thermalism is a dynamic component within the College of Health Sciences of the University of Bordeaux.

### "IIMT" INTERUNIVERSITY INSTITUTE FOR SPA MEDICINE: PRESENTATION

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Keywords: spa training; spa medicine, health education, prevention

The IIMT (Institut Interuniversitaire de Médecine Thermale or Interuniversity Institute for Spa Medicine), founded in 2018, is a no-wall institute co-piloted par the Clermont Auvergne University (UCA) and the Grenoble Alpes University (UGA). L'IIMT constitutes an innovative and experimental partnership tool aimed at boosting university involvement in the field of hydrotherapy in the Auvergne-Rhône-Alpes region (mainly expertise, teaching, research).

IIMT was born with the spa plan of the Auvergne-Rhône-Alpes region and founded by local authorities (Region, Vichy & Vichy Community). Its governance is based on a Scientific Committee, composed of 6 members, 3 from UCA and 3 from UGA, which meets every month.

IIMT is part of a spa regional network of complementary partnerships including:

• FTARA (Fédération Thermale Auvergne-Rhône-Alpes or Regional Spa Federation of

Auvergne-Rhône-Alpes) for elected representatives of spa towns & spa medical establishments.

- Innovatherm for spa innovation in spa establishments.
- The trades and qualification campus « thermalisme, bien-être et pleine santé » (Spa, wellness, full health) devoted to non medical education in new spa jobs.
- Regional council services.

#### Main achievements of IIMT:

- Spa education and spa medical education in professional training schools : psychotherapists, osteopathic practitioners, physiotherapists, spa managers and in project for sports educators for disabled people.
- Contributing to compensate for the shortage of spa doctors through targeted training actions
  - participation in teaching the DIU (Inter University Diploma) of "medical practice in spas"
  - a M.D. thesis on a Spa medicine observatory (regional level) to know the level of heterogeneity of medical practices for arthrosis treatments, the demography and qualifications of spa physicians.
  - media communications to increase the attractiveness of spa medicine
- Contributing to the nomination dossier of the "Great Spas of Europe" at Unesco world heritage for describing the Outstanding Universal Value of spa medicine.
- Participating into two European programs: Innovaspa, Healps (Interreg Alpine Space : Healps2 Accueil | Facebook).
- Design and development of an original health education for prevention of chronic diseases in spas based on 6 days stays or included in the 3-weeks French traditional "spa cure". This "reborn healthy" program is an adapted 4P medicine in spas (4P means: Preventive Personalized Predictive Participative) with the aim to educate people for sustainably changing to a better and protective way of life for their health. It includes with spa treatments 5 different workshops on physical activity & sedentary, nutrition, stress & relaxation, environment, change management.

#### Other objectives of IIMT:

- Education of citizens in health prevention and "full health" in spa resorts.
- Federate existing thermal research centers and stimulate their creation in resorts where the medical and university environment allows it.

Fundings: Auvergne-Rhône-Alpes Regional Council, Vichy city, Vichy Communauty, Cneth (National Council for Spa Establishments).

#### TOWARDS NEW PROFESSIONS FOR A NEW FRENCH BALNEOLOGY

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Key words: Education; health promotion; physical activity; prevention

Aging-related disorders and chronic diseases represent two main issues in public health for our developed countries. In France, before the Covid-19 pandemic, balneology centers received about 600,000 patients per year for a 21-day stay. They include a majority of people over 60 years who present with chronic disorders. This stay is underutilized by our health system which is mainly focused on curative approaches and less performant in the field of prevention. The stop of thermal activities related to the Covid crisis offers us the opportunity for rethinking the position of balneology within our health system. Furthermore, this crisis strengthens the need for prevention and assistance in the general population.

For more than 20 years the "Institut du Thermalisme", University of Bordeaux, develop its activities of education and research in the field of balneology. Converted to a health campus from 2018 this structure hosts students beginning their training in health careers (medicine, pharmacy, odontology, physiotherapy...) and proposes three professional licenses related to the balneology sector. We aim to mount a new course which could represent a bridge between these two training courses and an opportunity for closing chronic gaps in student achievement. Importantly, there is clearly a need for new professions dedicated to patient'education, at the crossroads of health, nutrition, gerontology and sport, especially for patients with chronic disorders and the elderly. The training of this new category of professionals dedicated to prevention may constitute a response to our current public health problems such as population aging, increase in diseases frequency due to physical inactivity-associated problems and unhealthy nutritional habits: obesity, type 2 diabetes, cardiovascular disorders, or cancers.

The thermal stay would represent the ideal site for that type of intervention as a new stage within the public health armentarium besides hospital- and home-based care. During the stay, these new professionals could provide to patients and their caregiving therapeutic education, counselling regarding living conditions, nutrition and adapted physical activity, primary or secondary prevention. Other sites could be used for that purpose such as for instance retired homes, enterprises, or sport clubs. Thus, we currently design a new course entitled Prevention Health Behavior and Aging in connection with medical studies (especially for non-elected medical students) which is also proposed to a large series of studient profiles. This new job position could be identifyied as a "health coach" "nutrition health coordinator" "life coach" and would open new avenues for students. Within the context of the University of Bordeaux we plan to open this new experimental course in September 2022. It will directly offer a job (after two-years of study) or allow the access to our professional licences in relation with balneology that are associated with a high rate of employability. Dax is a perfect place with regards to the number of fields of practical experience (numerous thermal facilities, a general hospital, or the unique Alzheimer village in France).

### TRAINING OF SPA CENTERS STAFFS TO IMPLEMENT A THERAPEUTIC PATIENT EDUCATION PROGRAM IN FRANCE

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In 1996, WHO defined Patient Therapeutic Education as non-medical therapy aimed at helping patients with chronic pathology to cope with their disease independently.

In France, the HPST act "Loi Hôpital-Patient-Santé-Territoires" and the numerous texts that have followed since 2009, require anyone involved in a therapeutic education program to be trained in the practices of TPE during less 40 hours.

It is within this regulatory framework that training has been set up for players in balneology, in particular by the Institute of Thermalism, in order to train all those who will have to intervene in the implementation of a TPE program.

In addition, the TPE programs in France are closely supervised by the legislator with precise conditions of implementation and coordination and with the obligation of a declaration to the Health Regional Agencies (administrative authority) before implementation.

In this restrictive regulatory context, French spa centers, with the help of Afreth (French Association for Thermal Research), designed a number of programs for patients undergoing spa treatment for three weeks on a wide variety of conditions (nutrition, rheumatic, skin, venous conditions, psychotropic drugs withdrawal, .... Some of these programs have been or are currently being evaluated through clinical studies, with the support of Afreth.

In conclusion, the Institute of Thermalism, has largely contributed to the establishment of this 40-hour certificate as to date 240 persons (60 working in thermal centers) have been trained by this university structure representing.

If the TPE programs are supported by the Health Insurance in health establishments in France, the programs with similar objectives implemented in the thermal centers have to be supported mainly by the patient.