Protocols and self-checking plans for the safety of post-COVID-19 balneotherapy

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Abstract. During the COVID-19 pandemics, balneotherapeutic establishments were closed in Italy like in the rest of Europe. The Italian Foundation for Research in balneotherapy (FoRST) was asked to prepare a safety protocol to be proposed to the National Health Authorities to allow the establishments to restart their activity when possible, under safe conditions (the so-called Phase-2). The group of experts proposed the following hygienic and sanitary protocols of risk management for the initial reopening of the balneology settings in Italy. The plan aims to define the operating procedures to be implemented at the balneology establishments for the beginning of Phase-2 and to keep them constantly updated in the different periods that will characterize Phase-2 in relation to the trends of the disease. To this end the procedures, defined on the basis of the scientific state-of-the-art available today, will be updated and revised from time to time whenever further scientific evidence and directives from the Health Authorities make it necessary and/or useful. (www.actabiomedica.it)

Key words: balneotherapy, COVID-19, Phase-2

Introduction

Mild respiratory diseases are caused by viruses of the Coronaviridae family that circulate in the human population (1). In contrast, SARS-CoV (Severe Acute Respiratory Syndrome Coronavirus) and MERS-CoV (Middle East Respiratory Syndrome Coronavirus) are transmitted from animals to humans and cause severe respiratory diseases (SARS and MERS) (2). There are no specific vaccines or antivirals against SARS, and therefore contrast to the spreading of these viruses is based on conventional control measures like social distance and patient isolation.

SARS-CoV-2, a novel coronavirus closely related to SARS-CoV, was isolated in patients with a lung disease emerged in China in 2019 (3).

Medical Balneology is the modern, evidence-based version of the classical European thermal medicine, one of the oldest forms of western medical therapy (4-6). The “Thermae”, as an integrated set of medical facilities and services based on a natural resource (the mineral water and its derivatives), offer therapy and rehabilitation, as well as maintenance of health conditions (7-13). At the Thermae people can learn a better lifestyle, exercise, reinforce their health conditions, recover and develop their physical capabilities, recover from injuries and disease, find relief from ailments. Depending on the type of water(s) and their specificities, skin (14-18), rheumatic (19-22), respiratory (23-28), inflammatory (29-31), vascular (33, 34), digestive (35), urinary (36), or metabolic (37, 38) conditions can be prevented/cured. Although natural mineral (thermal) waters have long been used as treatment for various diseases, their mechanisms of action
at the cellular and molecular levels are now becoming clear. With the huge progress of scientific medicine, the use of an apparently simple medium (mineral water) might seem unnecessary. In the age of personalized medicine, pharmacogenomics, metabolomics, lipidomics, and highly sophisticated diagnostic and surgical techniques, the role of the Thermae may appear at least obsolete. Instead, the explosion of chronic diseases and the increase of elderly people urgently pose to contemporary medicine the issue of reinforcing primary and secondary prevention, contrasting chronicity and facing polypathology that – altogether – represent nowadays the key words of the welfare systems. It is a true revolution that hits on the healthcare organization models, with the hospitals of the future exclusively focused on acute patients, and a well-organized network of not-hospitalized medical healthcare facilities that guarantee the necessary integrated approach to the patient, from prevention to rehabilitation. A great number of people in the word are taking the issues of health into their own control, at least in terms of proactive recovery and health programs, and one of the places they can do this is the contemporary Thermae. Medical Balneology, when done correctly under medical prescription, provide the benefit of integrated health maintenance, therapy and recovery. There is a huge overlap between proactive health maintenance and reactive sickness care. Contemporary balneology creates programs that combine proactive and reactive components of health. Often contraindicated in the acute phases of several diseases, balneological treatments – in their different applications, from hydrokinesis to aerosol and muds, integrated with classical physiotherapy, rehabilitation procedures and diet – can face several needs of low or medium intensity care of non-acute patients. Medical balneology leverages on the technical and classical know-how of medical hydrology combined, whenever necessary, with standard therapeutic treatments prescribed by medical staff and administered by appropriately trained professional and qualified operators. In line with this view for the future of the welfare systems, the World Health Organization (WHO) deemed it appropriate to include Medical Hydrology in the strategic lines for the 2014-2023 period. Reference standards for Medical Balneology can be found in the Italian Foundation for Thermal Medicine Research (FoRST), the French Association Francaise pour la Recherche Thermale (Afreth), the International Society of Medical Hydrology (ISMH), the World Federation of Hydrotherapy and Climatology (FEMTEC), and in the Hydroglobe Report (WHO).

The lockdown phase generated the suspension of all the balneological activities in Italy (like in most of the other countries in the world). However, SARSCoV-2 prevalent transmission by breath droplets together with the structural organization of most of the balneological establishments, with several therapies administered collectively or individually but in the same space, generated the need for adequate safety rules to face the post-Covid-19 reopening and activities all over the world. Here we report the rules that the protocols and self-checking plans for the hygenic and sanitary safety of post-covid-19 balneotherapy.

**Development of the protocol**

Given: i) the complex situation generated by the Covid-19 epidemics in the Country (39-42); ii) that balneotherapy establishments are health settings where National Health Service therapies included in the Essential Levels of Assistance (LEA) are provided; iii) the recommendations of the World Health Organization (WHO) and the decrees of the Italian Ministry of Health aimed at limiting the risks of the so-called Phase-2, a specifically identified Group of Experts proposed the following operational protocols for the management of Covid-19 risk during balneology treatments. Two preliminary definitions are necessary to better understand the document: **sanitization** is the combination, in sequence, of the cleaning and disinfection procedures; **PPE (Personal Protective Equipment)** refer to the relative guidelines published by the National Health Institute (Istituto Superiore di Sanità).
Balneology treatments

The Balneology treatments for the respiratory tract and ENT are:

Irrigations

Nasal showers
The nasal showers allow the delivery of mineral water, at different pressures and temperatures, and the mineral water gases in direct contact with the mucosal surfaces of the nasal cavities.

Micronized nasal showers
Variant to the nasal shower which, instead of using the water as it gushes out at the source, conveys inside the nostrils a nebulized consisting of aqueous particles producing the dilution and elimination of secretions present in the nasal pits and in the nasopharynx, given the ability of particles to penetrate anatomical districts that are not otherwise easily accessible. They are administered by nasal ampoules.

Inhalation therapies
Inhalations allow the active ingredients contained in mineral waters to be sent to the mucous membranes of the upper and lower respiratory tract and to the middle ear. There are different forms and methods of delivery of inhalation therapy and the classifications take into account the technical characteristics of the appliances (single, collective, steam, compressed air), the physical characteristics of the inhaled substances (size of inhaled water particles, presence of gas, temperature and pressure) and the chemical characteristics of the mineral waters used. The most important aspect of the classification consists of the physical characteristics and in particular the size of the particles of inhaled water. Particles with a diameter greater than 10 microns stop at the level of the upper airways (nose, pharynx and larynx), those with a diameter between 10 and 3 microns can reach the tracheobronchial mucosa, while only those of about 1 micron can reach the finest bronchial branches, down to the terminal bronchioles.

Four methods are essentially used:
- inhalations
- aerosols
- humages
- nebulizations

- Inhalations involve the use of devices capable of fragmenting mineral water into particles, forming a jet of steam which is inhaled by the patient. In direct-jet inhalations, the pressure of hot steam on mineral water generates the formation of water particles of the size of about one hundred microns. The jet is conveyed against filters or plates that eliminate larger particles obtaining a homogeneous fog. Partial cooling of the jet is also achieved, reaching an optimal temperature of 37-38 °C. The patient stands in front of the appliance, about 20-25 cm away from the spout and inhales the steam with his nose or mouth. No masks, nasal forks or mouthpieces are used.

- Balneological aerosols consist of fine particles of mineral water capable of reaching, based on their size, even the most distal branches of the bronchial tree. There are several devices for dispensing this method, which differ in the ways in which mineral water is fragmented and therefore in the size of the particles produced. The most common ones use compressed air at a pressure of 0.5-1 atmospheres to obtain particles of different diameters. The aerosol has a temperature corresponding to that of the water at the source and depending on the pathology to be treated, the patient can use a mask, a nasal fork or a mouthpiece connected, through a rubber fitting, to the regulator.

- Humages are inhalation techniques which consist in letting the patient take on the gaseous content which develops spontaneously from mineral waters. Unlike the methods described above, aqueous particles are very scarce. The most used waters are the sulphurous ones for the quality and quantity of the gas released. Direct (individual) and indirect (collective) humages are distinguished according to whether single appliances are used, or the gas is released into an environment by simple fall or by impact of the water against a solid surface.

- Nebulizations are collective treatments. Patients stay in an environment where mineral waters are
transformed into a mist of aqueous particles of various sizes and are mixed with any gas released by the mineral waters.

**Insufflation**

Insufflations use only the mineral water gases that are completely deprived of the aqueous particles in suspension. The gases are introduced both into the respiratory tree via the nasal route and, for endotympanic procedures, directly into the Eustachian tube by catheterization.

**Politzer:** this method which has the same purposes and characteristics as endotympanic insufflation, is used as an alternative to tubal catheterization in all situations where the introduction of the catheter into the nasal cavity is not possible or difficult, such as in children. It consists in the introduction of vaporized hydrogen sulphide in one nostril keeping the other closed. Patient rhythmical swallowing facilitates the penetration of the gas into the middle ear.

**Pulmonary ventilation**

Performed with an apparatus that delivers an aerosol, lung ventilation promotes, through controlled respiratory gymnastics, the improvement of respiratory function in chronic broncho-pulmonary pathologies. By law, in Italy it is the only balneo-therapy that can also include the use of drugs.

**Main technical characteristics of inhalation therapy equipments**

- **For INHALATIONS**
  - Stainless steel steam generator
  - Misting chamber with heat and humidity regulation device
  - Heat and corrosion resistant injector nozzle
  - Dispenser with breaker and adjustable ceramic terminal.

- **For AEROSOL**
  - Compressor for compressed air production for medical use (oil-less, with filters)
  - Mineral water flow system
  - Connecting tube(s)
  - Mask and / or nasal bifurcation

For MICRONIZED SHOWER
- Support for micronized shower connection pipes
- Non-toxic connection pipes for connection of compressed air and mineral water with ampoule
- Average operational temperature: 36°C
- Nasal ampoule

**Other balneology treatments**

**Balneotherapy**
It consists in the use of mineral baths, for healing purposes, of hot or artificially heated mineral waters. Among the various methods are the hydromassage, the vascular path and vascular gymnastics.

**Muds**
Peloids are natural or artificial products that derive from the mixing of mineral, sea, river or lake waters with inorganic, organic or mixed material of biological origin. They are used as compresses or for baths.

**Mineral water drinking (Hydropinotherapy)**
Hydropinotherapy consists of drinking mineral waters for therapeutic purposes. The cure consists in drinking given quantities of mineral water at a specific temperature, and according to times and modalities established by the medical prescription.

**Anthrotherapy**
Caves and stoves are collective balneology practices that involve exposure to variable temperatures and relative humidity rates, with prolonged stay and scarce air exchange.

**Vascular path**
Walkways along two pools containing mineral water, at least 80 cm deep, with a bottom suitable for vascular needs, with a temperature excursion of 5-10 °C, with a duration of 20 minutes and with the possible presence of ozone jets and lateral hydromassages at various heights.
**Vaginal irrigations and rectal showers**

They allow mineral waters to reach different temperatures and pressures, in direct contact with the vaginal and rectal mucous membranes. They are individual therapies, performed under medical supervision.

These definitions refer to and concern treatments envisaged, authorized and/or in some cases specifically included in the LEA (DPCM 12 January 2017).

**Operative protocols**

The organization chart of the persons responsible for implementing the protocol and verifying its correct execution is defined by each establishment and should in any case include the Property, the Prevention and Protection Service, the Occupational Doctor, the Spa Doctor and the Health Director.

The Employer defines the corporate Covid Unit, coordinated by a manager (Covid Surveyor, with a specific delegation from the Employer) in charge of collecting the evidences related to the implementation of the procedures and acting as a link between the general management, employees and users of the Balneology establishment. The purposes are:

- in light of the new Covid-19 prevention measures, collaborate in the definition or update of the Risk Assessment Document (RAD) and of the Prevention Plan adapted to the specifications of the balneology establishment by the Health Director;
- encourage the implementation of national or regional guidelines, contextualising them within the individual balneology establishment;
- facilitate homogeneous and coherent behaviors among the employees;
- represent a single reference figure available to all workers, avoiding uneven behaviors, while promoting staff training;
- Represent for the management the intermediate responsible for the implementation of operating procedures.

**The General measures include:**

- The Employer, through the Prevention and Protection Service and in collaboration with the Health Director and the Occupational Doctor, trains all workers (who will sign a specific training form) and implements all the applicable prevention and protection measures provided for by current legislation (including the use of specific PPE);
- The Employes, on the basis of the information and training received, will sign a commitment for a daily self-assessment of any onset of symptoms;
- The Employer, also through his delegates, defines the specific sanitisation procedures for the establishment, also providing periodic internal checks on the levels of sanitization;
- The Employer, also through his delegates, organizes the logistics of the changing rooms so as to guarantee the requisites of interpersonal distancing and to allow adequate and frequent sanitization interventions. To this end, he defines the maximum number of subjects present at the same time in each changing room, publicizes the rules by adequate advertising and implements an access control system that verifies when the maximum number of people has been reached; changing rooms furnishings must be organized in such a way as to facilitate spacing (benches, lockers, chairs, etc.);
- The Employer, also through his delegates, guarantees that all subjects who access the establishment are subjected to body temperature measurement by means of Thermoscan; for patients, the measurement is taken before the acceptance medical examination;
- The Employer, also through his delegates, makes disinfectant gel or hydroalcoholic solution for the hands available in all environments, using in any case no-touch dispensing or non-reusable bottles;
- The Employer, also through his delegates, communicates to the patient at the time of booking to come with his own surgical mask. However, disposable surgical masks must be available both at the entrance of the structure and in
other environments to be used in case of need (damage, loss, etc.);

- The Employer, also by means of his delegates, guarantees the recirculation of the air, favoring its replacement as per current regulations and guidelines (ISS COVID-19 Report, no. 5/2020) in all patients areas of the establishment (waiting rooms, medical toilets, treatment departments, changing rooms, etc.);
- The Employer, also by means of his delegates, guarantees that the furnishings, the deckchairs, the tables and the seats are pre-arranged so as to allow the physical spacing of at least 2 meters;
- The Employer, also through his delegates, favors the physical distance of at least 2 meters by organizing appropriate access rounds during the working hours; however, there can be exceptions in the case of patients using the same facilities (i.e. patients sharing the same room in the hotel);
- The Employer, also through his delegates, guarantees the individual use of the elevators and their periodic sanitization;
- The Employer, also by means of his delegates, displays signs on the rules of conduct for the public, showing the following list as a minimum:
  - do not drink from the same bottle / flask / glass, always using disposable glasses or a nominal or personalized bottle, and do not exchange objects with other people (towels, bathrobes, etc.);
  - prohibition to eat food in common or not specified areas;
  - store personal items and clothing in your bags;
  - immediately dispose the paper tissues or other used materials (patches, bandages, etc.);
  - wash your hands thoroughly and disinfect them with antiseptic gel;
  - do not touch your eyes, nose or mouth with unwashed / disinfected hands;
  - maintain an interpersonal distance of at least 2 meters;
- wear the surgical mask correctly, ensuring coverage of the mouth and the nose;
- avoid staying in common areas, always guaranteeing interpersonal distance.

**Specific measures for inhalation / ENT therapies and related departments**

The Employer, also through his delegates, guarantees that the following services are **NOT PROVIDED:**

- steam jet inhalations, as they are applied in the absence of customized dispensing devices (masks, nasal forks, mouthpieces) capable of limiting the potential viral spread from the patient to the environment. If the establishment has single, isolated workstations, this therapy is allowed, with complete sanitization of the environment between one patient and the next;
- collective therapies (collective humages, nebulizations);
- caves.

The Employer, also through his delegates, also guarantees that:

- all other inhalation therapies are carried out with respect for inter-individual distances (alternate occupation of individual workstations, with continuous and complete sanitization of unoccupied workstations);
- the Eustachian tube catheterization stations are completely sanitized between patients, with periodic internal controls;
- the pulmonary ventilation stations are completely sanitized patients, with periodic internal controls;
- the areas are equipped with efficient air exchange, as required by current legislation in order to ensure both air circulation and appropriate spare parts.

The spa doctor, during the acceptance visit, pays particular attention to recent anamnestic data in re-
lation to the known symptomatology of COVID-19 and/or known non protected contacts and, after having detected their absence, formulates the personalized therapeutic respiratory protocol for the patient, excluding collective therapies and steam jet inhalations (unless individual), evaluating their possible replacement with other means of inhalatory administrations (e.g. sonic aerosol or nasal showers, etc.).

The spa doctor is subject to the specific prevention and protection procedures identified by the employer, as also indicated by the national Guidelines.

**Measures for other balneology therapies and related departments**

All individual therapies are allowed. In all procedures assisted by technical and/or health personnel, these must wear the required PPE; patients must wear the surgical mask. Disinfection of the hands between one patient and another with alcohol-based gel and replacement of gloves is mandatory. These are specific cases:

**Mud-balneotherapy**

The patient is allowed to remove the mask during the shower. The service staff will take this into account by increasing the distance from the patient. The treatment is carried out in a single use cabin; the operator will wear all the PPE provided, always maintaining, when possible, the established interpersonal distance.

**Massage therapy**

Massage without gloves is allowed. Before the massage, the operator cleans and disinfects hands and the entire forearm up to the elbow; he/she repeats the operation at the end of the treatment. During the whole treatment, the operator wears the other expected PPE.

**Hydropinic therapies**

Inter-personal distancing is mandatory as per general rules, also favoring people stay in open spaces. In the case of use of closed rooms for hydropinic treatment, the Employer, also by means of his delegates, indicates the maximum number of people who can be present in each room at the same time, ensuring the minimum inter-personal distance of at least 2 meters. In these rooms, however, both air circulation and appropriate spare parts are guaranteed.

**Vascular paths**

The Employer, also through his delegates, guarantees interpersonal distancing by adopting suitable access criteria and rounds, based on the structural characteristics of the path itself; he also guarantees the sanitization of the handrail between one patient and the next unless the patient wears disposable gloves from the beginning of the treatment or that the washing of the hands and forearms has been carried out.

**Pools**

The National Health Institute stated that “there is no evidence that COVID-19 can be spread to humans through the use of swimming pools or whirlpools (x). Correct operation, maintenance and adequate disinfection of swimming pools and whirlpools ensures the inactivation of the SARS-CoV-2 virus” (FAQ - ISS of 16.04.2020). The Employer, also through his delegates, guarantees that:

- the minimum interpersonal distance of 2 meters is maintained; for this purpose, the maximum number of people who can simultaneously access the pool is defined; a system is also implemented to monitor the number of visitors present and block access to the pool when the maximum allowed number of people is reached;
- an effective air extraction system is active, as per current legislation;
- the pool area is equipped with advertising of the hygiene standards to be adopted, and with supervising personnel.

**Hydrokinesitherapy**

Hydrokinesitherapy is based on therapeutic exercise in water. This practice is carried out by a qualified physiotherapist who might work with the patient in water or outside the pool. If procedures requiring a reduced distance between the patient and the therapist cannot be avoided, the operator AND the patient must wear PPE.

Therefore the Employer, also through his delegates, guarantees that:
• patients shower before entering the pool;
• the hydrokinesitherapeutic activity takes place in dedicated pools (or in dedicated hours), allowing the physiotherapist remain out of the water;
• the operators wear the PPE required;
• in the case of rehabilitation in water of a disabled person, the presence of the therapist is allowed in water. The safety of the patient and therapist are guaranteed by PPEs that MUST be worn by both;
• at the end of each treatment the pool handrails and all tools used are sanitized.

Gyms and Rehabilitation Gyms

The employer, also through his delegates, guarantees that gym activities (such as motor rehabilitation or free attendance by users of the facility) are carried out:
• in environments where the maximum number of people who can be present at the same time has been defined;
• in environments where appropriate advertising indicates the hygienic-sanitary behavior to be maintained;
• in environments with adequate air circulation and appropriate air exchange;
• following correct environmental sanitation of the equipment used;
• with respect for interpersonal distancing

To this end, the staff uses the PPE provided and monitors users’ compliance with what is established and indicated in the signs. Users must wear masks. The spacing of at least 2 meters between patients must be ensured.

Conclusions

The recommendations collected here constitute a contribution to the recovery of activities at high interest for public health but also with a relevant economic impact. These indications, drawn from international scientific evidences, must of course be coordinated and adapted with the national and regional regulations which characterize phase 2 and which are periodically updated. In this perspective, a contribution from Italian authors appears useful not only for the long tradition in balneotherapy but also because the regions of northern Italy were the first areas of Europe to be affected by the COVID-19 pandemic and among those with the greatest number of cases and deaths (39-42).

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References

1. Corman VM, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu DKW, Bleicker T, Brünink S, Schneider J, Schmidt ML, Mulders DGJC, Haagmans BL, van der Veer B, van den Brink S, Wijsman L, Goderski G, Romette JL, Ellis J, Zambon M, Peiris M, Goossens H, Reusken C, Koopmans MPG, Drosten C. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro Surveill. 2020 Jan 25;(3).
2. Fehr AR, Channappanavar R, Perlman S. Middle East Respiratory Syndrome: Emergence of a Pathogenic Human Coronavirus. Annu Rev Med. 2017 Jan 14;68:387-399.
3. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Niu P, Zhan F, Ma X, Wang D, Xu W, Wu G, Gao GF, Tan W; China Novel Coronavirus Investigating and Research Team. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med. 2020 Feb 20;382(8):727.
4. Gutenbrunner C, Bender T, Cantista P, Karagülle Z. “A proposal for a worldwide definition of health resort medicine, balneology, medical hydrology and climatology”. Int J Biometeorol. 2010 Sep;54(5):495-507. doi: 10.1007/s00484-010-0321-5.
5. Kwiatkowski F, Mouret-Reynier MA, Duclos M, et al. Long-term improvement of breast cancer survivors’ quality of life by a 2-week group physical and educational intervention: 5-year update of the ‘PACThe’ trial. Br J Cancer. 2017;116(11):1389-1393. doi:10.1038/bjc.2017.112.
6. Morer C, Roques CF, François A, Forestier R, Maraver F. The role of mineral elements and other chemical compounds used in balneology: data from double-blind randomized clinical trials. Int J Biometeorol. 2017;61(12):2159-2173. doi:10.1007/s00484-017-1421-2.
7. Valeriani F, Margarucci LM, Romano Spica V. Recreational Use of Spa Thermal Waters: Criticisms and Perspectives for Innovative Treatments. Int J Environ Res Public Health. 2018;15(12):2675. Published 2018 Nov 28. doi:10.3390/ijerph15122675.
8. Margarucci LM, Romano Spica V, Gianfranceschi G, Valeriani F. Untouchability of natural spa waters: Perspectives for treatments within a personalized water safety...
plan. Environ Int. 2019;133(Pt A):105095. doi:10.1016/j.
envint.2019.105095
9. Guida M, Di Onofrio V, Gallè F, et al. Pseudomonas aeruginosa in Swimming Pool Water: Evidences and Perspectives for a New Control Strategy. Int J Environ Res Public Health. 2016;13(9):919. Published 2016 Sep 15. doi:10.3390/ijerph13090919
10. Romano Spica V, Gallè F, Baldelli G, et al. Swimming Pool safety and prevention at the time of Covid-19: a consensual document from GSMS-SItI. Ann Ig. 2020;32(5):439-448. doi:10.7416/ai.2020.2368
11. Pasquarella, C., Veronesi, L., Napoli, C., Castaldi, S., Pasquarella, M.L., Saccani, E., Colucci, M.E., Auxilia, F., Gallè, F., Di Onofrio, V., Tafuri, S., Signorelli, C., Liguori, G., 2014. What about behaviours in swimming pools? Results of an Italian multicentre study. Microchem. J. 112, 190–195. https://doi.org/10.1016/j.microc.2013.09.024.
12. Liguori, G., Castaldi, S., Signorelli, C., Auxilia, F., Pasquarella, C., Alfano, V., Saccani, E., Visciano, A., Fanti, M., Spinelli, A., Pasquarella, M.L. Hygienic Risks in Swimming Pool: Knowledge and Behaviours of Consumers of Three Structures in Crema, Parma and Naples. Ann Ig. Jul-Aug 2007;19(4):325-325.
13. Valeriani F, Gianfranceschi G, Romano Spica V. The microbiota as a candidate biomarker for SPA pools and SPA thermal spring stability after seismic events. Environ Int. 2020;137:105595. doi:10.1016/j.envint.2020.105595
14. Karagüle MZ, Karagüle M, Kılıç S, Seviç H, Dündar C, Türkoğlu M.: "In vitro evaluation of natural thermal mineral waters in human keratinocyte cells: a preliminary study. Int J Biometeorol. 2018 Sep;62(9):1657-1661. doi:10.1007/s00484-018-1565-8. Epub 2018 Jun 2. PubMed PMID: 29860536.
15. Carbajo JM, Maraver F: “Salt water and skin interactions: new lines of evidence”. Int J Biometeorol. 2018 Aug;62(8):1345-1360. doi: 10.1007/s00484-018-1545-z.
16. Zöller N, Valesky E, Hofmann M, Bereiter-Hahn J, Berndt A, Kaufmann R, Meissner M, Kippenberger S. "Impact of clays improve the endurance of loaded inspiratory muscles in heavy smokers. Int J Biometeorol. 2019;63(9):1209-1216. doi:10.1007/s00484-019-01737-7.
17. Thea Magrone, Mauro Galantino, Nunzio di Bitonto, Laila Borraccino, Gerardo Chiaramonte, Emilio Jirillo. “Effects of thermal water inhalation in chronic upper respiratory tract infections in elderly and young patients” Immunity & Ageing (2016) 13:18 DOI 10.1186/s12979-016-0073-0.
18. Monica Neri, Luigi Sansone, Luisa Pietrasanta, Aliaksei Kisialiou, elosia Cabano, Marina Martini, Matteo A. Russo, Donatella Ugolini, Marco Tafani, Stefano Bonassi. "Gene and protein expression of CXCR4 in adult and elderly patients with chronic rhinitis, pharyngitis or sinusitis undergoing thermal water nasal inhalations" Immunity & Ageing (2016) 13:18 DOI 10.1186/s12979-016-0073-0.
19. Francesca Benedetti, Sabrina Curreli, Selvi Krishnan, Sergio Davinelli, Fiorenza Cocchi, Giovanni Scapagnini, Robert Gallo, Davide Zella. “Anti-inflammatory effects of H2S during acute bacterial infection: a review”. Benedetti et al.
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31. Rinaldi L, Gobbi G, Pambianco M, Micheloni C, Mirandola P, Vitale M. “Hydrogen sulfide prevents apoptosis of human PMN via inhibition of p38 and caspase 3”. Lab Invest. 2006 Apr;86(4):391-7. PubMed PMID: 16446703.

32. Mirandola P, Gobbi G, Sponzilli I, Pambianco M, Malinverno C, Cacchioli A, De Panfilis G, Vitale M. “Exogenous hydrogen sulfide induces functional inhibition and cell death of cytotoxic lymphocytes subsets”. J Cell Physiol. 2007 Dec;213(3):826-33. PubMed PMID: 17516567.

33. Bucci M, Papapetropoulos A, Velleco V, Zhou Z, Pyrioso chou A, Roussos C, Roviezzo F, Brancacone V, Cirino G. “Hydrogen sulfide is an endogenous inhibitor of phosphodiesterase activity”. Arterioscler Thromb Vasc Biol. 2010; DOI: 10.1161/atvbaha.110.209783.

34. Carpentier PH, Blaise S, Satger B, et al. A multicenter randomized controlled trial evaluating balneotherapy in patients with advanced chronic venous insufficiency. J Vasc Surg. 2014;59(2):447-454.e1. doi: 10.1016/j.jvs.2013.08.002

35. Bothe G, Coh A, Auinger A. “Efficacy and safety of a natural mineral water rich in magnesium and sulphate for bowel function: a double-blind, randomized, placebo-controlled study”. Eur J Nutr. 2017 Mar;56(2):491-499. doi:10.1007/s00394-015-1094-8.

36. Nouvenne A, Meschi T, Prati B, Guerra A, Allegri F, Vezzoli G, Soldati L, Gambaro G, Maggiore U, Borghi L. “Effects of a low-salt diet on idiopathic hypercalciuria in calcium-oxalate stone formers: a 3-mo randomized controlled trial”. Am J Clin Nutr 2010; 91:565-70.

37. Schnebelen-Berthier C, Negro N, Jaruga A, Roques CF, Lecerf JM. Long term effect of spa therapy combined with patient education program on subjects with overweight and obesity - A controlled study. Obes Res Clin Pract. 2019;13(5):492-498. doi:10.1016/j.orcp.2019.06.005

38. Chary-Valckenaere I, Locuelle D, Jay N, et al. Spa therapy together with supervised self-mobilisation improves pain, function and quality of life in patients with chronic shoulder pain: a single-blind randomised controlled trial. Int J Biometeorol. 2018;62(6):1003-1014. doi:10.1007/s00484-018-1502-x

39. Signorelli C, Scognamiglio T, Odone A. COVID-19 in Italy: impact of containment measures and prevalence estimates of infection in the general population. Acta Biomed. 2020 Apr 10;91(3-S):175-179. doi: 10.23750/abm.v91i3-S.9511

40. Odone A, Delmonte D, Scognamiglio T, Signorelli C. COVID-19 deaths in Lombardy, Italy: data in context. Lancet Public Health. 2020 Apr 24. pii: S2468-2667(20)30099-2. doi: 10.1016/S2468-2667(20)30099-2.

41. Signorelli C, Odone A, Gianfredi V, Bossi E, Bucci D, Oradini-Alacreu A, Frascella B, Capraro M, Chiappa F, Blandi L, Ciceri F. The spread of COVID-19 in six western metropolitan regions: a false myth on the excess of mortality in Lombardy and the defense of the city of Milan. Acta Biomed. 2020; 91(2) doi 10.23750/abm.v91i2.9600

42. Boccia S, Ricciardi W, Ioannidis JPA. What Other Countries Can Learn From Italy During the COVID-19 Pandemic. JAMA Intern Med. 2020 Apr 7. doi: 10.1001/jama.2020.1447. [Epub ahead of print]