The Dead Sea, A Unique Natural Health Resort

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The Dead Sea area is unique for its combination of natural resources that are unparalleled anywhere else on earth. They include sun rays that are weakened due to the longer path they have to travel to reach the Dead Sea shores, which are 415 m below sea level, and the dispersion of the sun rays on their way by a misty cloud overhanging the sea most of the year. The attenuation is in inverse relation to the length of the ray; as a result, the shorter ultraviolet B rays are attenuated to greater extent than the longer UVA rays (12% and 3.8% on average respectively). This difference in solar radiation intensity provides a major therapeutic advantage, since damage to the skin after solar exposure increases as the UVB solar rays become shorter. However, the effective wavelength for suppressing psoriatic skin lesions is around 311 nm, a range at the longer wavelength end of the UVB scale [1,2]. In addition to the unique composition of sun rays, the low altitude of the area results in a high atmospheric pressure (37 mmHg), which is approximately 5% higher than at sea level. As a result the partial oxygen tension at the Dead Sea is about 7–8 mmHg higher than at zero altitude; this has important therapeutic implications for patients with hypoxic heart and lung diseases, as will be specified below. The water in this lake, as compared to seawater, contains an unusual composition and unusually high concentrations of cations, e.g., magnesium, sodium, calcium, and anions such as phosphorus, bromide and chloride. These raise the density of the water to about 1.237 kg/L, causing people bathing in the lake to float on rather than swim in the water. Certain minerals in the water have been shown to penetrate the skin, which may contribute to its healing effect [3]. Nanotechnological techniques are presently being explored to improve the penetration of therapeutic agents through the skin.

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The natural climatotherapy at the Dead Sea is both highly effective and almost without side effects

Mineral and sulphur-containing natural springs are found along the shores. Also, black mud, which contains medicinal antibacterial and hyperemic properties [4], is extracted from the shores of the lake. With regard to climate, a dry stable temperature reaches high levels during midsummer, while an extremely low rainfall is recorded in the very moderate winter. The elevated barometric pressure, high temperature and low humidity have been shown to have a favorable effect on patients with various rheumatic diseases. The air, which is unpolluted due to the scarcity of industry and vehicular traffic in the area, and non-allergenic due to the sparse vegetation, is of benefit to allergic individuals, especially asthmatic patients.

Dead Sea climatotherapy

In view of the rising costs of prescribed medicines and the public's higher awareness regarding their possible toxic side effects, exposure to the natural elements as part of alternative modes of therapy is gaining more and more appeal. Since the natural features of the Dead Sea area have been found to affect...
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an increasing number of chronic diseases, climatotherapy, balneotherapy and thalassotherapy are gaining in popularity among both Israeli and foreign patients. A recently discovered anti-aging effect of the minerals in the Dead Sea water and medicinal mud on the human skin supported by gene expression studies [Maor et al, personal communication] is expected to add to the appeal of the Dead Sea among healthy people striving to slow down the aging process of the skin. With regard to safety, properly dosed exposure has been found to be perfectly suitable for people of any age, including pregnant women and small children.

Therapeutic effect on skin diseases

The beneficial effect of the lake's climatotherapy for dermatologic diseases such as psoriasis, eczema, lichen planus and vitiligo has been amply documented in a multitude of scientific publications over the last 40 years. As a result it was established that while both the solar component and immersion in Dead Sea water are effective, the climatotherapeutic effect of the former on psoriasis is far more striking than the latter [5]. Optimum results are achieved by a short immersion in the Dead Sea water followed by sun exposure of 1 hour 30 minutes once in the morning and once in the afternoon during the extended summer months [6]. The optimum solar exposure time for psoriasis is between March and August [7].

A meteorological station located on the roof of a building on the southwestern shore of the lake performs continuous UV monitoring, providing online data on the daily solar ambient radiation intensity [8]. Moreover, recent studies with radiosensitive detector badges placed on the body determined the actual amount of radiation absorbed on the skin surface of patients bathing in the sun [Giryes H, personal communication]. A computerized program was designed and installed in the solarium at Ein Bokek (the resort area where most hotels are located) to enable patients to regulate their own initial daily exposure time based on their skin type and on data of the radiation intensity measured on the specific hour of the day of exposure. The actual amount of energy to which the individual's body is exposed by these methods is about one-third of the amount applied in artificial irradiation therapy regimens. The therapeutic results lead to an 80–90% remission, which compares favorably with artificial irradiation modes [9]. In a recent study of 64 German psoriasis patients we found that the mean duration of remission is 6 months [10]. It has also been shown that climatotherapy at the Dead Sea where patients mix socially with other guests in a hotel atmosphere, as compared to conventional modes of a clinic and sometimes hospital facilities, has psychological benefits that often have a positive effect on their self-image and consequently on their quality of life [Amir M, et al., personal communication].

The effect on the pathogenesis in psoriasis

One of the authors (M.D.) published a study in 2003 examining the effect of this therapy on the pathologic changes and immunologic modulation in the skin of psoriatic patients [11]. Histologic examination of the skin revealed normalization of the characteristic pathologic changes found in psoriasis, while immunologic studies showed a major reversal in immunologic activation.

Preliminary data show that when Dead Sea climatotherapy was combined with topical administration of calcipotriol, applied before and during the climatotherapy, the time needed to obtain optimum results in the clearance of psoriatic lesions was reduced [Abels D, et al., personal communication].

Other skin diseases

Dead Sea climatotherapy has also been found to exert a favorable effect in atopic dermatitis [Giryes H, et al., personal communication], as well as vitiligo [12], dyshydrotic eczema, lichen planus, ichthyosis, parapsoriasis, pityriasis rubra pilaris, urticaria pigmentosa (adult type), necrobiosis lipoidica, circumscribed scleroderma, alopecia areata, lichen sclerosus and atrophicus and granuloma annulare [13]. Additional studies to confirm these data are warranted.

The unparalleled combination of natural features in the Dead Sea area provides therapeutic modalities for a wide variety of chronic skin, joint, lung, heart and eye diseases

Dead Sea climatotherapy for mycosis fungoides

Hodak et al. [14] reported that Dead Sea climatotherapy is an effective and well-tolerated treatment for patients with patch-stage mycosis fungoides, a common form of malignant cutaneous T cell lymphoma. Of the 12 patients in their study, 11 had a complete or almost complete clinical response, and of 9 patients in whom skin biopsies were performed, 6 exhibited histopathologic clearing. The mean duration of remission was 5 months [14].

The Dead Sea area as an international center for climatotherapy

Repeated studies have shown that even severe forms of psoriasis that otherwise require hospitalization and often need systemic medications such as oral retinoids, methotrexate or cyclosporine respond strikingly to climatotherapy, let alone milder forms. And all this without having to risk the potential side effects associated with the administration of these systemic medications. As a result thousands of patients from Israel and from Europe – e.g., Germany and Scandinavian countries, supported by their respective health insurance funds, and recently also countries of the former Soviet Union – flock to the Dead Sea to take advantage of this mode of treatment. (The Israeli health insurance funds finance a 4 week climatotherapy treatment regimen for qualifying patients with psoriasis.)
The economics of Dead Sea climatotherapy
A study performed by the Swiss Psoriasis Association showed that while Dead Sea climatotherapy is as effective as artificial treatments in severely affected psoriasis patients, it is less expensive when comparing overall expenditures for both modes of therapy [15]. In view of its cost-effectiveness, health insurers in several European countries subsidize Dead Sea climatotherapy – Germany and Norway for skin diseases and Norway for joint diseases.

Dead Sea sun exposure and skin damage
In climatotherapy the skin is exposed only to a fraction of the energy to which the body is exposed in artificial radiation therapy protocols, which makes this natural therapy incomparably safer. The main potential deleterious effects of repeated climato-therapeutic exposures are long-term hazards such as loss of the skin’s elastic tissue and other features of skin aging. On the other hand, it is an open question whether repeated exposure to Dead Sea climatotherapy increases the risk for the development of skin cancer. This problem was addressed in an early paper by Frentz et al. [16], who found a significant increase in skin cancer in their patients and considered this a serious drawback of Dead Sea climatotherapy. However, this finding derived from an uncontrolled study in which the patients, whose information was collected from a national health registry, had in addition to Dead Sea climatotherapy also been exposed to artificial radiation and various systemic treatments. David and co-authors [17] reexamined this question in 1999–2000 in a multicenter controlled cross-sectional study on 460 psoriatic patients and 738 controls. The aim of the study was to determine the prevalence of solar damage and skin cancer among Israeli patients who were exposed to Dead Sea climatotherapy on a repeated basis. The results showed that solar elastosis, lentigines and facial wrinkles were more common among psoriatic patients exposed to Dead Sea climatotherapy, but there was no evidence that Dead Sea climatotherapy was associated in these patients with an increase in skin cancer of any type, including malignant melanoma [17]. Surprisingly, the rate of solar keratosis, which represents a pre-malignant lesion, was lower among the psoriatic group as compared to controls. This finding suggests that either the psoriatic skin carries some protective features against the solar-based development of malignant skin tumor [18] or the specific attenuation of solar irradiation present in the area, being more prominent in the shorter UVB waves, has a less damaging effect than regular sun rays.

Future studies
While psoriasis, being a more prevalent disease, has been studied in detail, other skin diseases in which Dead Sea climatotherapy has been shown to have a suppressive effect have not been examined as thoroughly. The following topics warrant further investigation:

• Pharmacology: It has been shown that the unique salt concentration present in the lake water adds to the immunomodulatory effect of the solar irradiation, but detailed pharmacologi- cal studies are lacking. New immunologic agents such as Amevive®, Enbrel®, etc., that have appeared on the market have proven to be effective against psoriasis but are very expensive. In contrast, Dead Sea climatotherapy has been proven no less effective and far less costly. It is reasonable to explore combination therapies between these new agents and Dead Sea climatotherapy with the aim of reducing the dosage and hence the cost of the immunomodulatory agents and possibly improve the effectiveness of the treatment.
• Genetics: It is recognized that psoriasis can occur in different genetic dispositions, but it is not known whether climatotherapeutic outcome can be predicted on the basis of the type of genetic aberration. The gathering of such information, currently underway in an increasing number of diseases, would add to a better understanding of the pathogenesis of disease and the mechanism of action of the treatment.

Application to other skin diseases
It is evident that the therapeutic effect of Dead Sea climato-therapy on a number of skin diseases is well established and studies performed during recent years have advanced our knowledge about optimal therapeutic conditions, the mechanism of action of the therapeutic effects, and the duration of remissions in psoriatic patients. On this basis it can be expected that Dead Sea climatotherapy – if instituted in a proper way – is as effective as other artificial modes of actinic therapy or chemical treatments applied to a variety of skin diseases mentioned above, and in fact much safer while patients function as hotel guests in a relaxed environment, which in itself raises their psychological well-being and consequently their quality of life.

Rheumatic diseases
Despite the many published reports on the effectiveness of balneotherapy in a broad spectrum of rheumatic diseases in spa resort areas, mainly in Europe, the number of prospective controlled randomized studies is small and there are many operational and methodological problems that cannot always be solved satisfactorily. During the last 15 years a group of researchers from the Soroka University Hospital and the Ben-Gurion University Faculty of Health Sciences have conducted clinical studies assessing the effectiveness of spa therapy in various inflammatory arthritides such as rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis, as well as non-inflammatory arthritides such as osteoarthritis and fibromyalgia [19-29]. Treatment modalities that were assessed and compared included mud pack therapy, bathing in mineral spring and bathing in Dead Sea water. Table 1 summarizes the main results of spa therapy in inflammatory arthritides. The most important conclusions from these studies were:

• Significant improvement in most of the assessed clinical parameters; the improvement was usually of short duration, not lasting more than a few months.
• Despite the prevailing opinion that balneotherapy is contraindicated in active inflammatory arthritides, we found...
that patients with active rheumatoid arthritis or active psoriatic arthritis also show improvement with these modes of therapy.

- Balneotherapy cannot be recommended as a substitute for drug therapy, only as an adjuvant therapy.
- The clinical improvement is usually not associated with an improvement in laboratory parameters such as erythrocyte sedimentation rate or C-reactive protein [19-24].

Table 2 summarizes the main results of spa therapy in non-inflammatory arthritides. The main points arising from these studies were that the results are less impressive than those reported for patients with inflammatory arthritides, and any improvement reported was usually of shorter duration than in inflammatory arthritides, lasting from 1 to 3 months.

Two additional studies that were conducted outside the Dead Sea area in order to neutralize the beneficial effects of the unique climate conditions demonstrated that Dead Sea mud therapy in rheumatoid arthritis and Dead Sea salt in osteoarthritis are more effective than false mud therapy and table salt (NaCl) respectively.

Moreover, chronic pain relief might be an additional effect of hydrotherapy, balneotherapy, and spa treatment [28]. In fibromyalgia patients Dead Sea balneotherapy was shown to have a favorable effect on their symptomatology, leading to an improvement in their quality of life [25-29].

Hypoxic conditions

Being the lowest point on earth, the Dead Sea area has unique natural conditions, including an abnormally high partial pressure of oxygen, which is beneficial for patients with hypoxic pulmonary, cardiac or combined conditions.

Lung diseases

After a short stay in the area patients with advanced chronic obstructive pulmonary disease show an improvement in pulmonary function, such as PaO\textsubscript{2} and PaCO\textsubscript{2}. 6 minute walking distance and sleep oximetry. Many of these patients, who at normal altitude require artificial oxygen supplementation, were found to increase their exercise capacity at the Dead Sea without requiring artificial aids [31,32].

Pediatric cystic fibrosis patients were shown to benefit from spending the winter holidays at the Dead Sea; they were able to increase their functional capacity with a reduced need for artificial oxygen. A group of 73 CF patients who participated in a winter camp at the Dead Sea demonstrated an improvement both in their mean SaO\textsubscript{2} (96.4–97.1, P < 0.0001) as well as in their forced vital capacity and forced expiratory volume in the first second (P < 0.05) [33,34]. No evidence was found of cross-infection with resistant bacteria such as Pseudomonas aeruginosa, which is a potential threat in CF patients. Since CF patients who congregate closely together are at particular risk, we specifically looked for evidence of this pathogen [35]. Studies performed by Falk and colleagues [36] showed that a brief stay of non-oxygen-dependent CF patients in the Dead Sea area resulted in an enhanced VO\textsubscript{max}. During sub-maximal exercise their blood oxygen improved at the Dead Sea area compared to sea level. Additionally, there was a trend for decreased VO\textsubscript{2} in absolute val-

Table 1. Details of clinical studies in inflammatory arthritides

<table>
<thead>
<tr>
<th>Disease</th>
<th>Authors</th>
<th>Study design</th>
<th>Mode of therapy by group*</th>
<th>No. of patients</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>Sukenik et al. [19]</td>
<td>Prospective, randomized, single-blind (observer)</td>
<td>a. Mud pack</td>
<td>40</td>
<td>Improvement in all three treatment groups</td>
</tr>
<tr>
<td>RA</td>
<td>Sukenik et al. [20]</td>
<td>Prospective, randomized, single-blind (observer)</td>
<td>a. Dead Sea (control)</td>
<td>36</td>
<td>Improvement in three treatment groups</td>
</tr>
<tr>
<td>PsA</td>
<td>Sukenik et al. [21]</td>
<td>Prospective, randomized, single-blind (observer)</td>
<td>a. Dead Sea (control)</td>
<td>166</td>
<td>Better improvement in treatment group</td>
</tr>
<tr>
<td>PsA</td>
<td>Sukenik et al. [22]</td>
<td>Prospective, randomized, single-blind (observer)</td>
<td>a. Mud packs + sulphur pool + Dead Sea</td>
<td>28</td>
<td>Improvement</td>
</tr>
<tr>
<td>PsA</td>
<td>Eltayam et al. [23]</td>
<td>Prospective, randomized, single-blind (observer)</td>
<td>a. Dead Sea (control)</td>
<td>42</td>
<td>Better and prolonged effect in treatment group</td>
</tr>
<tr>
<td>AS</td>
<td>Codish et al. [24]</td>
<td>Prospective, randomized, single-blind (observer)</td>
<td>a. Control (no therapy)</td>
<td>28</td>
<td>Improvement in both groups</td>
</tr>
</tbody>
</table>

* Groups were assigned various treatments, denoted a, b, c and d.
RA = rheumatoid arthritis, PsA = psoriatic arthritis, AS = ankylosing spondylitis.

Table 2. Details of clinical studies in non-inflammatory arthritides

<table>
<thead>
<tr>
<th>Diseases</th>
<th>Authors</th>
<th>Study design</th>
<th>Mode of therapy by group</th>
<th>Number of patients</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteoarthritis</td>
<td>Sukenik et al. [25]</td>
<td>Prospective, randomized, single-blind (observer)</td>
<td>a. Sulphur pool</td>
<td>40</td>
<td>Improvement in all three treatment groups</td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>Buskila et al. [29]</td>
<td>Prospective, randomized, single-blind (observer)</td>
<td>a. Sulphur pool</td>
<td>48</td>
<td>Better improvement in treatment group</td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>Buskila et al. [29]</td>
<td>Prospective, non-randomized, single-blind (observer)</td>
<td>a. Mud pack + sulphur pool</td>
<td>28</td>
<td>Improvement in both groups</td>
</tr>
</tbody>
</table>

CF = cystic fibrosis
ues and as a percentage of maximal capacity along with a trend for increased ventilatory reserve. These results suggest that even a brief stay at the Dead Sea may have physiologic benefits for young CF patients with moderate to severe lung disease [36].

Heart diseases

Family physicians and cardiologists are often confronted with questions concerning the effects and safety of descent to the Dead Sea area for cardiac patients. Studies conducted on ischemic heart disease patients and on patients with congestive heart failure show that descent to the Dead Sea had no detrimental effects on exercise performance capacity and there was no clinical evidence of ischemia in patients with coronary heart disease. In fact, in patients with congestive heart failure, significant short-term beneficial effects were noted during their stay in the Dead Sea area: systolic blood pressure decreased at rest and increased during a sub-maximal exercise test, while rest and exercise oxygen saturation increased, as did treadmill exercise time, rest and exercise cardiac output, and VO$_{2}$max ($P < 0.05$) [37,38]. In contradistinction to high altitude, where deterioration in ischemia and heart failure occurs, the elevated barometric pressure present at the Dead Sea, associated with an increased partial pressure of oxygen present in the inspired air, results, by increasing arterial oxygen tension, in the observed salutary effects on the heart. The increase in cardiac output at rest was associated with a decrease in systolic blood pressure in patients with congestive heart failure, implying that reduction in afterload at the Dead Sea may have contributed to the improvements observed. The high magnesium content present in the Dead Sea brine and haze can be an additional factor in the reduction of observed arterial pressure and the afterload reduction, thus facilitating myocardial work and reducing oxygen demand.

When blood pressure changes were compared in 72 hypertensive and normotensive patients staying in Beer Sheva (barometric pressure 745 mmHg) and at the Dead Sea (barometric pressure 800 mmHg), the sojourn at the Dead Sea showed an average decrease of 17 mmHg, a change that diminished slightly after 10 days stay at the Dead Sea. These data indicate that there is no contraindication for hypertensive patients to be exposed to climatotherapy at the Dead Sea [39].

Eye diseases

It has been shown that the environment of the Dead Sea has a positive effect on uveitis, a chronic inflammatory eye disease. In a cohort of 50 patients exposed to Dead Sea climatotherapy, there was a significant short and long-term amelioration of the inflammation during their stay in the Dead Sea area and a slight dissipation of the effect during the intervals between visits. Sixty-four percent of the patients reported that they required less medication and had fewer and milder attacks of uveitis following the visits. This improvement is considered to be related to the effect of UVB light on chronic ocular inflammation by its suppressive immunomodulatory effect [40].

Conclusions

The information provided in this paper show that Dead Sea climatotherapy can provide an effective but temporary remission in a number of diseases, being a mode of treatment that does not put a major strain on the patient, is undertaken in a pleasant environment and, if applied according to recommended schedules, carries minimal complications. Other diseases and treatment combinations are presently under investigation.

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A man should never be ashamed to own he has been in the wrong, which is but saying, in other words, that he is wiser today than he was yesterday.

Alexander Pope (1688-1744), British poet, and translator of Homer’s Iliad and Odyssey

Capsule

Decreased synthesis of fatty acids

The protein known as TRB3 is a pseudokinase (a kinase-like protein that lacks kinase activity) synthesized in fasting animals. TRB3 modulates insulin signaling and is related to a Drosophila protein that coordinates mitosis and morphogenesis during development. Qi and team found that over-expression of TRB3 in mice confers resistance to diet-induced obesity. This effect appears to be the result of decreased activity of acetyl-coenzyme A carboxylase (ACC) and consequent decreased synthesis of fatty acids. TRB3 directly interacts with ACC to promote its degradation via the E3 ubiquitin ligase constitutive photomorphogenic protein 1. Understanding the regulation of lipid metabolism may promote therapeutic strategies for the control of obesity.

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