

Different Modalities of Spa Therapy for Skin Diseases at the Dead Sea Area

Sima Halevy, MD; Shaul Sukenik, MD

Background: Balneology and spa therapy, although not accepted as well-established treatment modalities in dermatology, are used throughout the world. The therapeutic properties for skin and rheumatic diseases of the Dead Sea area may be attributed to unique climatic characteristics and unique natural resources. The mechanisms by which a broad spectrum of diseases are alleviated by spa therapy may involve mechanical, thermal, and chemical effects.

Objective: To review and discuss various spa therapy modalities, used at the Dead Sea area for a wide spectrum of skin diseases.

Conclusions: Existing evidence indicates the therapeutic potential of Dead Sea spa therapy modalities for psoriasis and psoriatic arthritis. A beneficial effect is hinted at for other skin diseases, but the absence of relevant methodological and clinical information precludes the drawing of any scientific conclusions. It is essential to establish therapeutic guidelines to determine the optimal treatment modality for each disease, and the optimal protocol of each treatment component, adjusted individually for each patient, with respect to remission and long-term adverse effects.

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BALNEOLOGY AND spa therapy, although not accepted as well-established treatment modalities in dermatology, are used throughout the world.¹⁻³

The therapeutic properties for skin and rheumatic diseases⁴⁻¹⁰ of the Dead Sea (DS) area, situated 400 m below sea level, have been known since ancient times. These therapeutic properties may be attributed to unique climatic characteristics and natural resources,⁴⁻⁶ including meteorological variables, attenuation of UV,^{11,12} DS water (with its unparalleled salinity and unique composition), sources of natural thermomineral waters, the DS mineral mud, increased bromine content of the air, and a high selenium content of local drinking water. The possible role of psychological influences in the DS area cannot be overlooked.

MODALITIES OF SPA THERAPY AT THE DS AREA

Various spa therapy modalities are used at the DS area.^{10,13,14} These may be classified as heliotherapy (sun exposure), thalassotherapy (bathing in DS water), balneotherapy (immersion in baths and pools of

thermomineral water), pelotherapy (heated DS mud pack therapy), and climatotherapy (using atmosphere, temperature, humidity, barometric pressure, and light).¹³ In many studies climatotherapy at the DS area is referred to as a therapy consisting of sun exposure (heliotherapy) and bathing in DS water (thalassotherapy). Heliotherapy is carried out over a period of 3 to 4 weeks, with a gradual increase in sun-exposure time. The sun-dosage schedule is determined in accordance with the patient's skin type. Thalassotherapy⁴⁻⁶ is carried out by gradually increasing bathing time to a maximum of 1 hour per day. There are variations, modifications, and combinations of these spa therapy modalities. The DS spa therapy modalities may be combined with conventional topical medications, including emollients and noncorticosteroid preparations, salicylic acid, tar, and sulfur, in varying concentrations and combinations. Systemic drugs are not usually used during DS spa therapy for skin diseases.

INCLUSION AND EXCLUSION CRITERIA AND ADVERSE EFFECTS OF DS SPA THERAPY

Psoriasis is the disease most frequently treated by DS spa therapy, followed by atopic der-

From the Departments of Dermatology (Dr Halevy), and Internal Medicine (Dr Sukenik), Soroka University Medical Center, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel.

matitis and vitiligo. The DS spa therapy is also used for a small group of patients with other skin diseases, including acne vulgaris, dyshidrotic eczema, lichen planus, ichthyosis vulgaris, early-stage mycosis fungoides, pityriasis rubra pilaris, urticaria pigmentosa (adult type), necrobiosis lipoidica, circumscribed scleroderma, alopecia areata, lichen sclerosus and atrophicus, and granuloma annulare.¹⁴

Exclusion criteria for climatotherapy include systemic lupus erythematosus and other photoaggravated dermatoses, skin malignancies, acute skin infections (viral and bacterial), and immunodeficiency diseases. General contraindications include severe psychiatric conditions, acute alcoholic states, epilepsy, cardiac dysrhythmias, and inadequate balance. Contraindications for balneotherapy include severe varicose veins, nonhealed wounds, and hypersensitivity to mineral baths.¹⁴ Patients suffering from acute and subacute dermatitis are prohibited from bathing in DS water.¹⁰

Adverse effects of climatotherapy, consisting mainly of sunburn and other photosensitivity reactions (8.2% and 5%, respectively), have been observed in only a few patients.¹⁴ Exfoliative dermatitis developed in 1 case.¹⁵ Balneotherapy may cause a thermal reaction manifested primarily by exacerbation of joint pain and fatigue.

POSSIBLE MECHANISMS OF THE EFFECTIVENESS OF SPA THERAPY AT THE DS AREA

The mechanisms by which a broad spectrum of diseases are alleviated by spa therapy have not been fully elucidated. They probably incorporate mechanical, thermal, and chemical effects.^{1,8,9} Chemical effects of the DS spa therapy were evidenced by *in vivo* and *in vitro* studies,¹⁶⁻²¹ which disclosed increased levels of minerals that may play a role in cell proliferation and differentiation.²²⁻²⁴ Anti-inflammatory and immunomodulatory effects⁸ involving various cell lineages, inflammatory cytokine release, and cytokine receptor modulation²⁵⁻³⁰ may be induced by the thermal effects of spa therapy. Bathing in high concentrations of salt solutions may trigger the elution of various chemotactic and proinflammatory mediators (ie, elastase and cytokines) from the affected skin of patients with psoriasis, contact dermatitis, and atopic dermatitis.³¹⁻³³ Furthermore, bathing in tap water or salt solutions (including DS salts) has recently been associated with the increased photosensitivity of the skin to UV-B irradiation, and may contribute to the efficacy of balneophototherapy.^{34,35}

SPA THERAPY FOR PSORIASIS AT THE DS AREA

Various studies^{4,14,15,36-48} have indicated that different DS spa therapy modalities are effective in the treatment of psoriasis. Most types of psoriasis, except generalized pustular psoriasis, responded to treatment.¹⁰ Psoriatic erythroderma was successfully treated by heliotherapy in the DS area.⁴⁸ Until recently, most of these studies have consisted of clinical observations and descriptive rather than well-controlled studies. A review of the main clinical studies on DS spa therapy for psoriasis is presented later and in the **Table**.

The pioneering pilot studies of Dostrovsky et al³⁶ and Dostrovsky and Shanon³⁷ elucidated the therapeutic effect of helio-balneotherapy for psoriasis in the DS area. Avrach³⁸ and Montgomery³⁹ reported a beneficial effect in large groups of patients with psoriasis (577, 1052, and 1631, respectively) treated at the DS area.

Retrospective studies^{15,40,41} on 94, 110, and 1448 patients with psoriasis, respectively, treated at the DS area revealed a beneficial effect at the end of treatment in 81% to 88% of the patients, defined as complete clearing (95%-100% improvement), excellent improvement (80%-95% improvement), and marked improvement. The study groups consisted of selected patients with psoriasis,¹⁵ patients with psoriasis enrolled in a dermatology clinic at the DS from March 1983 to June 1983,⁴⁰ and a cohort of consecutive patients with psoriasis treated at a DS psoriasis clinic.⁴¹ Although most of the patients suffered from psoriasis vulgaris or plaque-type psoriasis, some heterogeneity with respect to the type of psoriasis was observed.⁴⁰ Furthermore, there were no uniform criteria for the extent of skin involvement prior to DS spa therapy (ie, >50 cm² involvement of skin area¹⁵; an average of 29% skin involvement⁴⁰; and $\geq 7\%$ involvement in 76% of the patients⁴¹). Heterogeneity with respect to the country of origin (Israeli and non-Israeli)⁴¹ and the duration of treatment (4 weeks,¹⁵ 14-42 days [mean, 26 days],⁴⁰ and 28 days⁴¹) was also observed. The treatment protocol⁴⁰ consisted of sun exposure (initial exposure of 10-20 minutes twice a day, depending on the skin type, with an increase in increments of 10 minutes each day until a maximum of approximately 6 hours a day) and bathing in the DS (initial bathing of 5 minutes, twice a day, with an increase in increments of 5 minutes every 3 days until a maximum of 30 minutes, twice a day). Topical adjuvant therapy consisted of emollients with or without nonsteroid ointments (containing salicylic acid, tar, and sulfur). In 1 of the series,⁴⁰ no significant improvement was observed in many patients until the third or fourth week. No significant associations were found with sex, previous DS spa treatments, prior hospitalization for psoriasis, prior psoralen-UV-A therapy, or history of arthritis.⁴¹ Determination of the individual UV sensitivity index (defined as the lowest exposure time to a UV radiation source, which produced erythema with defined border 24 hours later) by Azizi et al¹⁵ revealed a more favorable result of the DS climatotherapy in patients with psoriasis with high UV sensitivity index (≥ 90 seconds) compared with low UV sensitivity index (30 seconds).

A retrospective study by Giryes et al⁴² disclosed a similar efficacy of climatotherapy compared with a combination of climatotherapy and balneotherapy performed for 3 weeks in patients with psoriasis vulgaris. Climatotherapy given to 38 patients without joint involvement consisted of sun exposure and bathing in the DS. A combination of climatotherapy and balneotherapy was used in 80 patients with joint involvement. The regimen of balneotherapy consisted of heated DS mud packs and thermal baths. The mean (\pm SD) percentage reduction of the psoriasis area and severity index (PASI) score did not differ significantly between the groups (88.5% \pm 11.6% and 91.5% \pm 10.5%, respectively).

Dead Sea (DS) Spa Therapy Modalities for Psoriasis*

Source, y	No. of Patients	Type of Psoriasis	DS Spa Therapy Modality	Duration	Adjuvant Therapy	Skin Evaluation	Results, %
Azizi et al, ¹⁵ 1982	94	Plaque type	Sun exposure and bathing in the DS	4 wk	Emollients ± TNSP	3-Grade scale of response	Healing or marked improvement, 85
Abels and Kattan-Byron, ⁴⁰ 1985	110	Plaque/patchy, guttate, with or without PsA	Sun exposure and bathing in the DS	14-42 d (mean, 26 d)	Emollients ± TNSP	...	Complete clearing or excellent improvement, 81.4
Abels et al, ⁴¹ 1995	1448	Psoriasis vulgaris	Sun exposure and bathing in the DS	28 d	Emollients	...	Clearing of 80-100, 88
Giryès et al, ⁴² 1994	80	Psoriasis vulgaris and PsA	Sun exposure and bathing in the DS, mud packs, and thermal baths	3 wk	NS	PASI score, mean ± SD reduction	91.5 ± 10.5
	38	Psoriasis vulgaris	Sun exposure and bathing in the DS				88.5 ± 11.6
Sukenik et al, ⁴³ 1994	130	PsA	Sun exposure, bathing in the DS, mud packs, and sulfur baths	3 wk	Emollients ± TNSP	PASI score, mean ± SD reduction	93.3 ± 12.0†
	18		Sun exposure and bathing in the DS				96.0 ± 7.3†
Giryès et al, ⁴⁴ 1997	69	Psoriasis vulgaris	Climatotherapy and pretreatment	NS	NS	PASI score, mean	Decrease ($P < .001$)
	54		Climatotherapy and no pretreatment				Decrease ($P < .001$)
Even-Paz et al, ⁴⁵ 1996	15	Psoriasis, NS	Bathing in the DS and sun exposure (3 h)	28 d	Emollients	PASI score, mean reduction	90.2
	15		Bathing in the DS and sun exposure (4.5 h)				85.5
	15		Bathing in the DS and sun exposure (6 h)				88.9
Even-Paz et al, ⁴⁶ 1996	34	Plaque type	Sun exposure	4 wk	Emollients	PASI score, mean reduction	72.8
	15		Bathing in the DS				28.4
	32		Sun exposure and bathing in the DS				83.4
Halevy et al, ⁴⁷ 1997	13	Psoriasis vulgaris	DS salt baths	3 wk	Emollients	PASI score, mean ± SD reduction	34.8 ± 24.0
	12		Common salt baths				27.5 ± 18.3

*TNSP indicates topical nonsteroid preparations; PsA, psoriatic arthritis; NS, not specified; ellipses, not applicable; and PASI, psoriasis area and severity index. †A significant reduction in the number of inflamed joints.

The therapeutic role of DS spa therapy in patients with psoriatic arthritis was also shown in a prospective controlled study by Sukenik et al.⁴³ The study group was treated by a combination of sun exposure, bathing in the DS, mud packs, and sulfur baths, whereas patients treated traditionally only by sun exposure and bathing in the DS served as controls. The duration of treatment was 3 weeks. The mean (\pm SD) percentage reduction of the PASI score in the study group ($n = 130$) did not differ significantly from that of the control group ($n = 18$) ($93.3\% \pm 12.0\%$ and $96.0\% \pm 7.3\%$, respectively). A statistically significant improvement of the joint disease was observed in both groups ($P < .001$ and $P = .02$, respectively). However, reduction of spinal pain and increased range of lumbar spine movements were only observed in the study group. Despite the small number of patients in the control group and the fact that this study was not randomized, the age of the patients, the duration of psoriasis, and psoriatic arthritis as well as the use of nonsteroidal anti-inflammatory drugs and disease remitting drugs were similar in both groups.

The results of a retrospective analysis⁴⁴ implied that antipsoriatic pretreatment did not influence clearing of psoriasis vulgaris following DS climatotherapy (sun exposure and bathing in the DS). The study group consisted of 69 patients suffering from psoriasis vulgaris who were divided into 5 groups according to the antipsoriatic regimen used 4 weeks before DS climatotherapy (topical corticosteroids, calcipotriol, tar, salicylic acid ointment, or UV radiation). Fifty-four patients, who avoided using any medications 4 weeks prior to climatotherapy, served as a control group. Patients in all 5 pretreatment groups did not differ significantly with respect to sex, age, duration of disease, and climatotherapy. The PASI scores at the end of climatotherapy were significantly lower compared with PASI scores before climatotherapy in each study group ($P < .001$). However, no significant difference was observed in the PASI scores when the pretreatment groups were compared with the control group ($P > .05$).

A recent prospective study conducted by Even-Paz et al⁴⁵ determined the best sun-exposure times for psoria-

sis treatment at the DS area. The study included 45 Israeli patients with psoriasis (volunteers from the Israel Psoriasis Association) treated at the DS area in July and August 1994 for 28 days. Patients were assigned to 1 of 3 sun-exposure schedules with a maximum daily sun exposure of 3.0, 4.5, or 6.0 hours, respectively. The therapy regimen consisted of sun exposure (twice daily, gradually increased from a few minutes daily to the maximum), bathing in the DS (twice daily for 20-30 minutes), and emollients (used freely). At the end of the therapy, the mean percentage reduction in the PASI score did not differ significantly among the 3 groups (90.2%, 85.5%, and 88.9%, respectively). The weekly cumulative improvement was similar for all groups. The degree of improvement did not differ significantly in patients whose initial PASI score was 20 or more. The results indicate that the daily sun exposure for treatment of psoriasis at the DS area in July and August need not exceed 3 hours.

Another prospective study conducted by Even-Paz et al⁴⁶ indicated that sun exposure was the main factor producing beneficial results for psoriasis (plaque type) in DS spa therapy, and that bathing in DS water enhanced the effect of solar radiation. The study included 81 patients with psoriasis (volunteers from the Israel Psoriasis Association) allocated to 1 of the following groups: DS water bathing only (15 patients); sun exposure only (34 patients); and sun exposure combined with DS water bathing (32 patients). The DS water bathing was performed for 20 minutes twice daily in heated indoor pools. Sun exposure was done twice daily in solaria, with a gradual increase in exposure from a few minutes to 5.5 hours daily. The duration of treatment was 4 weeks. Adjuvant treatment consisted of emollients (used freely). Previous antipsoriatic treatments were discontinued 3 weeks before arrival at the DS area. The mean percentage reduction in the PASI score (recorded by 1 physician alone, or by 2 working together) was 28.4% in patients who only bathed in the DS water, 72.8% in those only sunbathing, and 83.4% in those doing both. There was no significant seasonal difference in the results related to the sun-exposure groups.

A recent prospective double-blind controlled study by Halevy et al⁴⁷ evaluated the sole therapeutic effect of DS salt in patients with psoriasis. The study included 25 patients with psoriasis vulgaris involving 15% or more of body area randomly allocated to 2 groups who were treated with either DS salt baths (13 patients) or common salt baths (12 patients). The treatment protocol consisted of once-daily salt baths that were heated to 35°C and of 20 minutes' duration, immediately followed by washing with tap water and lubrication of the skin (white soft paraffin, twice daily) for 3 weeks. Topical and systemic antipsoriatic therapy was withdrawn for 2 and 4 weeks, respectively, before starting the salt baths. In the DS bath salt and the common salt groups the mean PASI score at the end of treatment was significantly lower than the mean PASI score before treatment ($P = .005$ and $P = .001$, respectively). However, the mean percentage reduction in the PASI score at the end of treatment was higher in patients treated by DS bath salt compared with common salt (34.8% and 27.5%, respectively; $P > .05$). A similar trend was observed 1 month after termination of the treatment protocol (43.6% and 24%, respectively;

$P > .05$). The results imply a beneficial therapeutic effect to bathing with either DS bath salt or common salt as monotherapy for psoriasis vulgaris, although an enhanced beneficial effect was observed in patients treated with DS bath salts. Statistical significance was not reached, probably due to the small number of patients in our study ($P > .05$ and $P > .05$, respectively).

The studies reviewed earlier display heterogeneity with respect to study group composition (demographic variables, disease type, and severity), spa therapy modality (protocol, timing, and duration), and criteria used for assessment of disease severity and therapeutic results. Most lack relevant data regarding joint disease, previous treatments, and length of remission achieved. Evaluation of the relative effectiveness of various treatment modalities has been carried out in only a few recent studies. These limitations preclude comparative analyses of DS spa therapy for psoriasis.

SPA THERAPY FOR ATOPIC DERMATITIS AND OTHER SKIN DISEASES AT THE DS AREA

Two recent clinical observations^{14,49} provided evidence for the therapeutic potential of DS spa therapy for atopic dermatitis. Complete clearance of lesions was recorded in 90% of 1408 patients after 4 to 6 weeks' stay at the DS area (in 97% of the patients lesions cleared after 6 weeks and in 89% after 4 weeks). A reduction in itching was recorded during the first week of stay at the DS area. The percentage of patients who improved during the spring and summer was higher than in the autumn and winter.¹⁴ Girytes et al⁴⁹ reported the efficacy of DS climato-therapy for atopic dermatitis in 56 patients: 18 children younger than 18 years and 38 adults. The climato-therapy regimen consisted of daily sun exposure (maximum, 3-4 hours), bathing in diluted DS water or sweet water (20 minutes twice a day), and free application of emollients. Clinical evaluation was based on the index for Severity Scoring of Atopic Dermatitis. At the end of climato-therapy both groups showed a significant clearing of skin lesions, reductions in itch and sleep disturbances, and a significant decrease ($P < .001$) in the Severity Scoring of Atopic Dermatitis index.

Clinical observation of 102 patients with vitiligo treated by the DS climato-therapy⁵⁰ revealed beneficial results manifested by total or almost total repigmentation in 11% of the patients, significant repigmentation in 82.3%, partial repigmentation in 6.4%, and no change in 1% of the patients. Marked improvement was observed in 78% and 70% of the patients who stayed 4 to 6 weeks and 4 weeks, respectively, in the DS area.

Clinical observation of 86 patients treated for acne vulgaris in the DS area¹⁴ showed a significant improvement manifested by a reduced number of comedones and pustules.

Favorable effects of DS spa therapy were reported also for dyshidrotic eczema, lichen planus, ichthyosis, parapsoriasis, mycosis fungoides stage I, pityriasis rubra pilaris, urticaria pigmentosa (adult type), necrobiosis lipoidica, circumscribed scleroderma, alopecia areata, lichen sclerosus and atrophicus and granuloma annulare.¹⁴

CONCLUSIONS

Existing evidence indicates the therapeutic potential of DS spa therapy modalities for psoriasis and psoriatic arthritis. A beneficial effect is hinted at for other skin diseases, but the absence of relevant methodological and clinical information precludes the drawing of any scientific conclusions.

It is essential to establish therapeutic guidelines to determine the optimal treatment modality for each disease and the optimal protocol of each treatment component (dosing, frequency, duration, maintenance, or adjuvant medications), adjusted individually for each patient, with respect to remission and long-term adverse effects.

A large spectrum of variables should be integrated into the therapeutic guidelines of DS spa therapy, including the skin disease (type, severity, and duration), the skin type, history of skin cancer, chemical photosensitivity, associated diseases, drug intake and alcohol consumption, emotional state, response to previous treatments (conventional and nonconventional), and measurements of solar UV radiation during the DS spa therapy.⁵¹

The use of similar definitions and criteria in studies related to DS spa therapy modalities is mandatory for analysis and determinations of cost-effectiveness of DS spa therapy for skin diseases, compared with other conventional treatment modalities.

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Reprints: Sima Halevy, MD, Department of Dermatology, Soroka University Medical Center, Beer-Sheva 84101, Israel.

REFERENCES

- Lotti T, Freedman D. Balneology and spa treatments in dermatology: the European point of view. *J Eur Acad Dermatol Venereol.* 1994;3:449-450.
- Parish LP, Witkowski JA. Dermatologic balneology: the American view of waters, spas, and hot springs. *J Eur Acad Dermatol Venereol.* 1994;3:465-467.
- Routh HB, Bhowmik KR, Parish LC, Witkowski JA. Balneology, mineral water, and spas in historical perspective. *Clin Dermatol.* 1996;14:551-554.
- Even-Paz Z, Shani J. The Dead Sea and psoriasis: historical and geographic background. *Int J Dermatol.* 1989;28:1-9.
- Even-Paz Z, Efron D. The Dead Sea as a spa health resort. *Isr J Med Sci.* 1996;32(suppl 3):4-8.
- Even-Paz Z. Dermatology at the Dead Sea spas. *Isr J Med Sci.* 1996;32(suppl 3):11-15.
- Sukenik S, Shoenfeld Y. The Dead Sea is alive. *Isr J Med Sci.* 1996;32(suppl 3):1-3.
- Tishler M, Shoenfeld Y. The medical and scientific aspects of spa therapy. *Isr J Med Sci.* 1996;32(suppl 3):8-10.
- Sukenik S. Balneotherapy for rheumatic diseases at the Dead Sea. *Isr J Med Sci.* 1996;32(suppl 3):16-19.
- Abels DJ, Even-Paz Z, Efron D. Bioclimatology at the Dead Sea in Israel. *Clin Dermatol.* 1996;14:653-658.
- Kushlevsky AP, Slikin MA. Ultraviolet measurements at the Dead Sea and at Beer-sheba: biometeorological considerations. *Isr J Med Sci.* 1975;11:488-490.
- Kushlevsky P, Kudish A. Intercomparison of global ultraviolet B and A radiation measurements in the Dead Sea region (Ein Bokek) and Beer Sheva. *Isr J Med Sci.* 1996;32(suppl 3):24-27.
- Routh HB, Bhowmik KR. Basic tents of mineral water: a glossary of concepts related to balneology, mineral water, and the spa. *Clin Dermatol.* 1996;14:549-550.
- Shani J, Seidel V, Hristakieva E, Stanimirovic A, Burdo A, Harari M. Indications, contraindications and possible side-effects of climatotherapy at the Dead Sea. *Int J Dermatol.* 1997;36:481-492.
- Azizi E, Kushlevsky A, Avrach W, Schwach-Millet M. Climate therapy of psoriasis at the Dead Sea. *Isr J Med Sci.* 1982;18:267-270.
- Shani J, Barak S, Levi D, et al. Skin penetration of minerals in psoriasis and guinea pigs bathing in hypertonic salt solutions. *Pharmacol Res Commun.* 1985;17:501-512.
- Shani J, Sharon R, Koren R, et al. Effects of Dead Sea brine and its main salts on cell growth in culture. *Pharmacology.* 1987;35:339-347.
- Shani J, Sulliman A, Katzir I, Brenner S. Penetration of selected Dead Sea minerals through a healthy rabbit skin, from a sustained-release transparent varnish, as a prospective treatment for psoriasis. *J Eur Acad Dermatol Venereol.* 1995;4:267-272.
- Shani J, Even-Paz Z, Avrach WW, et al. Topical replacement therapy of psoriasis by Dead Sea salts, evaluated by scanning electron microscopy and x-ray fluorescence. *Dermatosen.* 1991;39:49-55.
- Shani J, Tur E, Wald E, et al. Computerized morphometry of psoriatic keratinocytes after bathing in the Dead Sea bath solutions. *J Dermatol Treat.* 1993;4:195-198.
- Shani J, Barak S, Ram M, et al. Serum bromine levels in psoriasis. *Pharmacology.* 1982;25:297-307.
- Vorhees JJ, Duell EA. Imbalanced cyclic-AMP and cyclic GMP levels in psoriasis. *Adv Cyclic Nucleotide Res.* 1975;5:735-738.
- Blondell JM. The anti-carcinogenic effect of magnesium. *Med Hypotheses.* 1980;6:863-871.
- Petrini M, Vaglini F, Carulli G, et al. Effects of lithium and rubidium on the differentiation of mononuclear cells. *Int J Tissue React.* 1986;8:391-392.
- Valitutti S, Costellino F, Musiani P. Effect of sulphureous "thermal" water on T lymphocytes proliferative response. *Ann Allergy.* 1990;65:463-468.
- Simonelli C. Come le acque sulfuree modulano il sistema immunitario. *Current.* 1994;1:15.
- Wollenberg A, Richard A, Bieber T. In vitro effect of the thermal water from La Roche-Posay on the stimulatory capacity of epidermal Langerhans cells. *Eur J Dermatol.* 1992;2:128-129.
- Sainte-Laudy J. Etude du pouvoir anti-degranulant de l'Eau d'Avene vis-à-vis de basophiles humains sensibilisés. *Int J Immunother.* 1987;3:307-310.
- Celerier P, Richard A, Litoux P, Dreno B. Modulatory effects of selenium and strontium salts on keratinocyte-derived inflammatory cytokines. *Arch Dermatol Res.* 1995;287:680-682.
- Arenberger P, Bartak P, Kemeny L, Ruzicka T. Cytokine receptor modulation: a possible balneotherapeutic effect in psoriasis. Paper presented at: Sixth International Psoriasis Symposium; July 20-24, 1994; Chicago, Ill.
- Wiedow O, Streit V, Christophers E, Stander M. Liberation of human leukocyte elastase by hypertonic saline baths in psoriasis. *Hautartz.* 1989;40:518-522.
- Wiedow O, Wiese F, Streit V, Kalm C, Christophers E. Lesional elastase activity in psoriasis, contact dermatitis, and atopic dermatitis. *J Invest Dermatol.* 1992;99:306-309.
- Wiedow O, Wiese F, Christophers E. Lesional elastase activity in psoriasis: diagnostic and prognostic significance. *Arch Dermatol Res.* 1995;287:632-635.
- Boer J, Schothorst AA, Boom B, Hermans J, Suurmond D. Influence of water and salt solutions on UVB irradiation of normal skin and psoriasis. *Arch Dermatol Res.* 1982;273:247-259.
- Schempp CM, Blumke C, Schopf E, Simon JC. Skin sensitivity to UV-B radiation is differentially increased by exposure to water and different salt solutions. *Arch Dermatol.* 1997;133:1610.
- Dostrovsky A, Sagher F, Even-Paz Z, et al. Preliminary report: the therapeutic effect of the hot springs of Zohar (Dead Sea) on some skin diseases. *Harefuah.* 1959;57:143-145.
- Dostrovsky A, Shanon J. Influence of helio-balneotherapy at the hot spring of Zohar (Ein-Bokek) on psoriasis: a further report. *Harefuah.* 1963;63:127-129.
- Avrach WW. Climatotherapy at the Dead Sea. In: *Proceedings of the Second International Symposium on Psoriasis, Stanford University.* New York, NY: Yorke Medical Books; 1976:258-261.
- Montgomery BJ. Bathing for psoriasis in the Dead Sea. *JAMA.* 1979;241:227-231.
- Abels DJ, Kattan-Byron J. Psoriasis treatment at the Dead Sea: a natural selective ultraviolet phototherapy. *J Am Acad Dermatol.* 1985;12:639-643.
- Abels DJ, Rose T, Bearman JE. Treatment of psoriasis at the Dead Sea dermatological clinic. *Int J Dermatol.* 1995;34:134-137.
- Giryas H, Halevy S, Sukenik S. Climatotherapy and balneotherapy for treatment of psoriasis vulgaris in the Dead Sea area. Paper presented at: Sixth International Psoriasis Symposium; July 20-24, 1994; Chicago, Ill.
- Sukenik S, Giryas H, Halevy S, et al. Treatment of psoriatic arthritis at the Dead Sea. *J Rheumatol.* 1994;21:1305-1309.
- Giryas H, Friger M, Sarov B, Halevy S. Does pretreatment of psoriatic patients influence climatotherapy at the Dead Sea? Biology and therapy of inflammatory skin diseases. Paper presented at: International Symposium at the Dead Sea; November 2-6, 1997; Dead Sea, Israel.
- Even-Paz Z, Efron D, Kipnis V, Abels DJ. How much Dead Sea sun for psoriasis? *J Dermatol Treat.* 1996;7:17-19.
- Even-Paz Z, Gumon R, Kipnis V, Abels DJ, Efron D. Dead Sea sun versus Dead Sea water in the treatment of psoriasis. *J Dermatol Treat.* 1996;7:83-86.
- Halevy S, Giryas H, Friger M, Sukenik S. Dead Sea bath salt for the treatment of psoriasis vulgaris: a double-blind controlled study. *Eur J Acad Dermatol Venereol.* 1997;9:237-242.
- Giryas H, Sukenik S, Halevy S. Clearing of psoriatic erythroderma following heliotherapy in the Dead Sea. *J Eur Acad Dermatol Venereol.* 1995;5:44-46.
- Giryas H, Friger M, Sarov B. Treatment of atopic dermatitis in the Dead Sea area: biology and therapy of inflammatory skin diseases. Presented at: International Symposium at the Dead Sea; November 2-6, 1997; Dead Sea, Israel.
- Seidel V, Hristakieva E, Harari M. Climatotherapy of vitiligo at the Dead Sea. *Dtsch Dermatol.* 1994;42:144-161.
- Kushlevsky A, Harari M, Kudish AI, et al. Safety of solar phototherapy at the Dead Sea. *J Am Acad Dermatol.* 1998;38:447-452.