

MCS) は重要である。患者との人間関係、信頼関係を構築することは医療を行う上で前提といえよう。患者へのインタビューがきちんとでき、患者から適切な情報を引き出すことができれば、多くの場合、診断や治療への道のりは近い。MCSを学んだことのない医療者は、このスキルを「口が上手な人」と形容するが、面白いことに実際の臨床で言語的コミュニケーションの占める範囲はわずか7%である。その多くは、表情やしぐさ等の非言語的コミュニケーション(55%)であったり、声のトーンや速さ等の準言語的コミュニケーション(38%)である。開放型質問や閉鎖型質問、沈黙・相槌・促し・繰り返し・要約などのスキルを駆使し、患者の解釈モデル(explanatory model)や物語を引き出されれば、質の高いケアにつながる。

### ◎多職種協働

現代の医療は、様々な職種の医療者によって提供されている。たった一人の匠の技で、もはや現代医療を実践することはできない。多職種チームがひとつの有機体となって患者のケアにあたるのが一般的である。いわゆる「チーム医療」だが、ビジネス業界などのチームとの大きな違いは、個々のメンバーが有資格者であり特殊技能を持つことだ。これを多職種協働(interprofessional work: IPE)という。地域医療の現場では、保健や福祉の専門家達とチームをつくりIPEを実践している。ここでは、他職種向けのコミュニケーション・スキルも必要となる。同じ現象をみても、それぞれの職種の教育の違いは、言葉の違いをうみ、アプローチの違いをうむ。CAMの治療者がメンバーに入れば、さらにアプローチは変わってくるであろう。患者に物語があるように、医師にも各職種にも、それぞれの物語がある。それぞれの物語が患者を中心に寄り添えば、患者中心の医療を実践可能にする。家庭医はIPEの実践において、リーダーシップを発揮できなければならない。

## 関連学会の動向

プライマリ・ケア領域の学会には、三大学会として、これまで日本プライマリ・ケア学会、日本家庭医療学会、日本総合診療医学会があった。2010年にこの三学会が合併して、日本プライマリ・ケア連合学会となった。専門医制度は日本プライマリ・ケア学会が実施していた制度を軸に実施されている。同学会の専門医取得には、内科・外科・小児科・精神科・救急など複数科での研修実績、症例報告50例の書類審査とともに、臨床能力評価試験(CSA: Clinical Skill Assessment)と論述試験を受けなければならない。CSAは近年医学部の学生に実施されているOSCE(Objective Structured Clinical Examination: 客観的臨床能力試験)をイメージしていただくと理解の助けとなる。受験者が医学生でなく経験豊富な臨床医なので、要求される能力は高い。例えば、生活習慣病の生活指導、禁煙指導、認知症への対応、小児へ

の対応などを実際の病院の診察室を試験会場とし模擬患者（simulated patientもしくはstandardized patient：SP）への診療をみることで評価する。ここでは勿論コミュニケーション・スキルなども評価の対象となる。また、シミュレーターを使っての心肺蘇生（ACLS：Advanced Cardiovascular Life Support）では気管内挿管や心臓マッサージ（胸骨圧迫）のスキルだけでなく、リーダーとなって適切なマネジメントができていかなども評価される。さらには豚足を使った小外科のスキルなど、そのほとんどが実践形式で評価される。今後の試験には日本家庭医療学会で積極的に行われてきたポートフォリオも取り入れられる。私は受験する側と評価する側の両者を体験したが、ともに大変な労力を要する専門医試験である。筆記試験だけでは総合的な臨床能力を評価することは極めて難しく、統合医療の専門医制度を検討するにあたっては参考にされたい。

## 家庭医の仕事場

上記のようなトレーニングを受けた家庭医やプライマリ・ケア医は、どのような仕事場で活躍しているのだろうか。

診療所の医師を想像することが最も簡単である。都会、郊外、下町、山村、離島など設定は様々であるが、外来診療を中心に、在宅医療、予防接種や健康教育などの保健活動、介護・福祉関係者との協働、学校医などに従事し地域医療を支えている。家庭医やプライマリ・ケア医の他、かかりつけ医、開業医、町医者、ホームドクターなどと呼ばれる医師達である。

小規模な病院では、内科医として外来・入院・在宅の診療を行っていることが多い。大学病院のような大病院では、総合診療科や総合内科という部門で外来と入院患者の診療にあたる。総合医と呼ばれる医師達である。総合医は、common diseaseから複数の健康問題を抱える患者、心療内科的な患者の治療、原因不明の疾患の精査、救急医療、専門科への振り分け業務など行っている。

ジェネラリストとしての臨床能力を身につけ、JICA・WHO・国境なき医師団など国際医療で活躍する者もいれば、健診や人間ドックなど予防医療の道を進む者もいる。個々の患者ではなく、地域住民全体の保健・医療・福祉の向上を目指し、公衆衛生の分野に興味を持ち、保健所・厚生労働省・WHOなど行政に関わる者もいる。

専門家と異なり、家庭医の仕事場は多様である。大事なことは、家庭医・プライマリ・ケア医・総合医と呼ばれる医師達の役割を最終的に決定づけるのは、地域であり、環境であり、住民である。家庭医は、与えられた環境やニーズを的確に把握し、自らの診療スタイルを決めていくのである。

## 家庭医療と統合医療

“Orthodox meets Alternative”と題して、BMJ誌から刊行された統合医療特集号は大変な話題と呼んだ。この特集号が21世紀の幕開けともいえる2001年の1月に刊行されたことは、新しい時代の予感を感じさせた。2羽のフラミンゴが首を絡ませた表紙の写真は印象的で、1羽は西洋医学、もう1羽はCAMなのであろう。この特集号でLeeとWeilによって統合医療という概念が紹介されたが、英国の医学雑誌ということもあり、“integrative medicine”でなく、“integrated medicine”と書かれていた。“integrated medicine”という言葉は、日本のプライマリ・ケア関係者の間では別の意味でよく知られている。医学書院から刊行されているプライマリ・ケア向け医学雑誌『JIM』のことである。『JIM』誌はJournal of Integrated Medicineを略で、雑誌の表紙には「プライマリ・ケア／総合診療のための『ジム』」と紹介されている。本学会が設立された時、略称がJIMであったので、これは用語をめぐって混乱を来たすのではないかと少し心配になった。余談ではあるが、これもまたプライマリ・ケアと統合医療に共通項が多いからであろう。

米国のアリゾナ大学にはProgram in Integrative Medicine (PIM) という部門がある。PIMは先のWeilが設立したことで有名で、統合医療のメッカである。私は2006年に訪問したが、アリゾナ大学の位置するTucsonは砂漠のオアシスといった印象で、CAM治療者のクリニックやオフィスが目立つ独特の町並みだ。PIMの臨床部門は“PIM Clinic”と称し、大学病院の中に一診療科として存在していた。カイロプラクティック、アロマセラピー、鍼、ホメオパシー、オステオパシー、ハーブ療法、ヨガなど複数のCAM治療者とネットワークを構築しながら診療が行なわれていた。このクリニックで、すなわち統合医療の現場で、学生教育も研修医教育もなされ、統合医療を学びたい医療従事者が世界中から集まってくるという。注目すべきは、PIM ClinicのMedical Directorが総合内科医であり、PIMの診療・教育・研究を統括するExecutive Directorが家庭医であったことだ。PIMを運営する二人がジェネラリストであることは大きな意味があると思われる。さらに驚かされたのが研修プログラムの名前が、Integrative family medicine (IFM) と呼ばれていること。IFMとはその名の通り統合医療を実践する家庭医を意味するが、これは統合医療を担う西洋医学側の医師として家庭医、総合医、プライマリ・ケア医などのジェネラリストが適していることを反映している。IFMプログラムはNCCAMがサポートしており、この当時すでにアリゾナ大学を始め米国の6大学ですでに始められていた。

プライマリ・ケアの視点からみると、欧米と日本ではCAMに接する態度が大きく異なる。欧米では家庭医が臨床の現場でCAMに興味を持ち、研究し、教育を担っていることが多い。たとえば米国の医学部では、CAMの授業を担当する教員はFamily medicine (家庭医療) もしくはGeneral medicine (総合医療) の所属者が最も多い。一方、日本では全80大学医学部のうちCAM関連の授業は69大学で実施さ

れているが、プライマリ・ケア関係者が実施しているのはわずか4校しかない。実際この結果を、同じTucsonで開催された第34回北米プライマリ・ケア研究会定例総会で発表すると、会場から驚きの声があがった。その意味は、「日本は米国よりもCAM利用者が多いのに、なぜ家庭医が興味を持たないのか？米国でCAMはすでにコモンなトピックとして扱われている」であった。

## おわりに

統合医療の担い手として、欧米では家庭医やプライマリ・ケア医に期待が寄せられている。家庭医療と統合医療の概念はよく似ており、家庭医療の臨床技能を少し広げ、CAMを考慮することで統合医療の実践につながる。統合医療の関係者には、家庭医療やプライマリ・ケアに興味を持っていただき、これまで蓄積された学問体系を知ってほしい。地域医療を支える家庭医・プライマリ・ケア医・総合医等の理解を促すことが統合医療推進の近道であることは言うまでもない。一方、家庭医にはCAMを利用する患者を受け入れ、向かい合ってほしい。欧米の家庭医達と同じようにCAMをコモンなトピックとして扱い、統合医療に関心をもっていたきたい。本稿が統合医療の発展に貢献し、日本の統合医療と家庭医療に橋をかける役割をしてくれればと願っている。

## Review Article

**Effectiveness of Aquatic Exercise and Balneotherapy:  
A Summary of Systematic Reviews Based on Randomized  
Controlled Trials of Water Immersion Therapies**Hiroharu Kamioka<sup>1</sup>, Kiichiro Tsutani<sup>2</sup>, Hiroyasu Okuizumi<sup>3</sup>, Yoshiteru Mutoh<sup>4</sup>, Miho Ohta<sup>5</sup>,  
Shuichi Handa<sup>3</sup>, Shinpei Okada<sup>6</sup>, Jun Kitayuguchi<sup>7</sup>, Masamitsu Kamada<sup>7</sup>,  
Nobuyoshi Shiozawa<sup>8</sup>, and Takuya Honda<sup>4</sup><sup>1</sup>Faculty of Regional Environment Science, Tokyo University of Agriculture, Tokyo, Japan<sup>2</sup>Department of Drug Policy and Management, Graduate School of Pharmaceutical Sciences, The University of Tokyo, Tokyo, Japan<sup>3</sup>Mimaki Onsen (Spa) Clinic, Tomi, Nagano, Japan<sup>4</sup>Department of Physical and Health Education, Graduate School of Education, The University of Tokyo, Tokyo, Japan<sup>5</sup>Laboratory of Aqua, Health, and Sports Medicine, Sapporo, Japan<sup>6</sup>Physical Education and Medicine Research Foundation, Tomi, Nagano, Japan<sup>7</sup>Physical Education and Medicine Research Center Unnan, Unnan, Shimane, Japan<sup>8</sup>Department of Longevity and Social Medicine, Okayama University Graduate School of Medicine,  
Dentistry and Pharmaceutical Sciences, Okayama, Japan

Received February 19, 2009; accepted July 2, 2009; released online October 31, 2009

**ABSTRACT****Background:** The objective of this review was to summarize findings on aquatic exercise and balneotherapy and to assess the quality of systematic reviews based on randomized controlled trials.**Methods:** Studies were eligible if they were systematic reviews based on randomized clinical trials (with or without a meta-analysis) that included at least 1 treatment group that received aquatic exercise or balneotherapy. We searched the following databases: Cochrane Database Systematic Review, MEDLINE, CINAHL, Web of Science, JDream II, and Ichushi-Web for articles published from the year 1990 to August 17, 2008.**Results:** We found evidence that aquatic exercise had small but statistically significant effects on pain relief and related outcome measures of locomotor diseases (eg, arthritis, rheumatoid diseases, and low back pain). However, long-term effectiveness was unclear. Because evidence was lacking due to the poor methodological quality of balneotherapy studies, we were unable to make any conclusions on the effects of intervention. There were frequent flaws regarding the description of excluded RCTs and the assessment of publication bias in several trials. Two of the present authors independently assessed the quality of articles using the AMSTAR checklist.**Conclusions:** Aquatic exercise had a small but statistically significant short-term effect on locomotor diseases. However, the effectiveness of balneotherapy in curing disease or improving health remains unclear.**Key words:** systematic review; aquatic exercise; randomized controlled trial; balneotherapy**INTRODUCTION**

Aquatic exercise has been referred to as pool therapy, hydrotherapy, and, in earlier literature, sometimes even as balneotherapy.<sup>1</sup> Exercise in warm water, usually called hydrotherapy or aquatic therapy, is a popular treatment for many patients with painful neurologic or musculoskeletal conditions.<sup>2</sup> The warmth and buoyancy of water may block nociception by acting on thermal receptors and mechanoreceptors, thus influencing spinal segmental mechanisms.<sup>3,4</sup> In addition, warm water may enhance blood flow, which is thought to help in dissipating algogenic chemicals, and

facilitate muscle relaxation. In addition, the hydrostatic effect may relieve pain by reducing peripheral edema<sup>5</sup> and by dampening sympathetic nervous system activity.<sup>6</sup>

Bathing in water (balneotherapy or spa therapy) without exercise has also been frequently used in alternative medicine as a disease cure. Spa therapy is a very popular form of treatment for all types of arthritis in many European countries, as well as in Israel and Japan.<sup>7,8</sup> In addition, recent reports have demonstrated that comprehensive health education, which includes lifestyle education and exercise in combination with spa bathing, has positive effects for middle-aged and elderly people.<sup>9,10</sup>

Address for correspondence. Dr. Hiroharu Kamioka, Ph.D, Faculty of Regional Environment, Tokyo University of Agriculture, Sakuragaoka 1-1-1, Setagaya-ku, Tokyo, Setagaya 156-8502, Japan (e-mail: h1kamiok@nodai.ac.jp).

Copyright © 2009 by the Japan Epidemiological Association

Although many studies have reported the effects of water exercise and balneotherapy, there is no review of systematic reviews of evidence from randomized controlled trials. The objective of this review was to summarize evidence for the effectiveness of aquatic exercise and balneotherapy and to assess the quality of systematic reviews based on randomized controlled trials of these therapies.

## METHODS

### Criteria for study inclusion

#### *Types of studies*

Systematic reviews based on randomized clinical trials (with or without a meta-analysis) were eligible.

#### *Types of participants*

Studies were not excluded based on the disease status of participants (ill vs healthy people).

#### *Types of intervention and language*

Studies that included at least 1 treatment group in which aquatic exercise or balneotherapy were included. A study of any type of exercise used in a therapeutic indoor pool or bath (range of motion exercise, dynamic exercise, aerobic exercise, immersion only, etc.) was acceptable. Studies had to include information on use of medication, alternative therapies, and lifestyle changes, and these had to be comparable among groups. When comparing different programs, type of exercise, type of water, water depth, and water temperature were considered. There was no restriction on the basis of language.

### Methods used to identify studies

#### *Bibliographic database*

We searched the following databases: Cochrane Database Systematic Review, MEDLINE via PubMed from 1990, CINAHL from 1990, Web of Science from 1990, Jdread II (in Japanese) from 1990, and Ichushi-Web (in Japanese) from 1990, for articles published up to August 17, 2008. The search was limited to studies published in or after 1990, the time period during which the systematic review methodology became accepted. All searches were performed by 2 hospital librarians who were qualified in medical information management and were highly trained in the retrieval of clinical trials.

#### *Search strategies*

The search strategies used for all databases contained the following elements and terms:

- (I) Search "aquatic therapy" or "aquatic exercise" or "water exercise"
- (II) Search ("water"[Majr] or "swimming"[Majr]) and exercise therapy/methods
- (III) Search "water gymnastic" or "water training" or "water aerobics" or "pool exercise" or "pool therapy" or "aerobic aquatics" or "hydrotherapy" or "thalassotherapy" or "aquatics" or "balneotherapy" or "spa therapy"

(IV) Search I or II or III

(V) Search I or II or III Limits: systematic reviews/meta-analysis

Only keywords related to intervention were used for searching. First, titles and abstracts of identified published articles were reviewed to determine the relevance of the articles. Next, the references in relevant reviews and identified randomized controlled trials (RCTs) were screened.

#### *Reference checking and hand searching*

We did not check the references of included studies, nor did we perform any hand searches or contact institutions, societies, specialists with expertise in aquatic exercise or balneotherapy, or the authors of included studies to identify any additional published or unpublished data.

### Review methods

#### *Selection of trials*

For the final selection of studies for this review, 2 authors (HK and TH) independently applied all criteria to the full text of the articles that had passed the initial eligibility screening (Figure 1). Disagreements and uncertainties were resolved by discussion between the authors.

Studies were selected when (1) the design was a systematic review of RCTs, and (2) one of the interventions was a form of aquatic exercise or balneotherapy. Effectiveness of cure or health improvement was used as a primary outcome measure. Health improvement was defined broadly, and encompassed improvements in blood pressure, serum lipid profile, immunity, and quality of life. We excluded systematic reviews of non-RCTs or observational studies. Trials that were excluded are shown, along with the reason for exclusion, in the Appendix.

#### *Quality assessment of included studies*

To ensure that variation was not caused by systematic errors in study design or execution, 2 review authors (MK and HK) independently assessed the quality of articles. A full quality appraisal of these papers was made using the AMSTAR,<sup>11</sup> which was developed to assess the methodological quality of systematic reviews. Disagreements and uncertainties were resolved by discussion between the review authors.

#### *Summary of studies and data extraction*

One author (HK) selected the summary from each of the structured abstracts and extracted the results for statistical analysis. The primary outcome measurement was always chosen for analysis.

#### *Benefits and harms*

The GRADE Working Group<sup>12</sup> reported that the balance between benefits and harms, quality of evidence, applicability, and the probability of baseline risk were all considered in judgments of the strength of recommendations. Adverse events and withdrawals are particularly important for researchers and users of clinical practice guidelines, and we present this information with the description of each article.

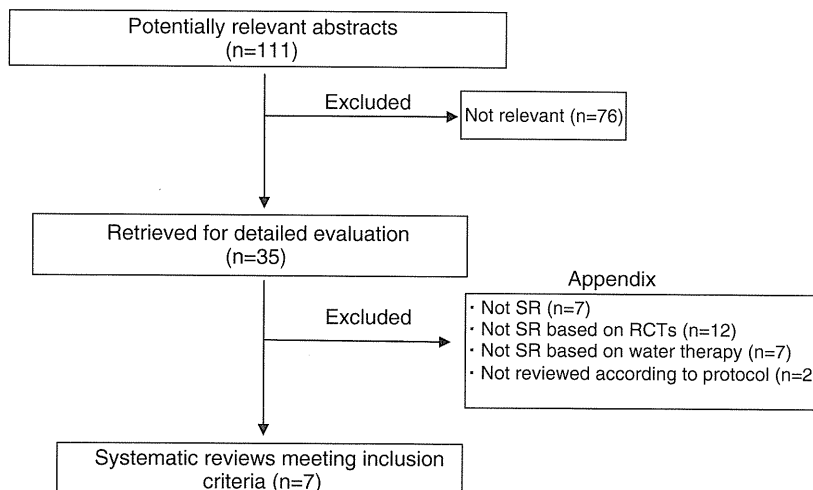


Figure 1. Flowchart of trial process  
SR: systematic review. RCT: randomized controlled trial.

## RESULTS

### Study characteristics

The literature searches identified 111 potentially relevant articles (Figure 1). Abstracts from those articles were assessed and 35 studies were retrieved for further evaluation (assessment of relevant literature). Twenty-eight publications were excluded either because they were not a systematic review (SR), not an SR based on RCTs, not an SR in which water was a factor, or were not reviewed according to protocol (see Appendix). Seven trials<sup>1,2,13-17</sup> met all inclusion criteria (Tables 1 and 2). These included 3 SRs on aquatic exercise (spa therapy)<sup>1,2,16</sup> and 5 SRs on balneotherapy<sup>13-17</sup>; one of these concerned both balneotherapy and spa therapy (with physiotherapy). The target diseases and disorders included knee and hip osteoarthritis,<sup>1,14,15</sup> rheumatoid arthritis,<sup>13</sup> low back pain,<sup>16</sup> and neurologic or musculoskeletal disease (ie, rheumatoid arthritis, fibromyalgia, low back pain, and osteoarthritis), along with a number of other diseases and disorders.<sup>2</sup> Studies on health improvement were also included.<sup>17</sup> The SRs of aquatic exercise showed a curative effect in all studies; however, the SRs of balneotherapy provided no clear evidence of curative effect (Table 3).

### Results of meta-analysis

Only 3 SRs<sup>1,2,16</sup> provided data that were suitable for statistical pooling. Regarding the effectiveness of aquatic exercise for the treatment of knee and hip osteoarthritis,<sup>1</sup> there was a small but statistically significant favorable effect for aquatic exercise on function ( $P < 0.001$ ; weighted standardized mean difference [SMD], 0.26; 95% confidence interval [CI], 0.11 to 0.42;  $n = 648$ ), quality of life ( $P < 0.05$ ; SMD, 0.32; 95% CI, 0.03 to 0.61;  $n = 599$ ), and mental health ( $P < 0.05$ ; SMD, 0.16; 95% CI, 0.01 to 0.32;  $n = 642$ ) measured immediately after the intervention period. Pain was assessed using a 100-mm visual analogue scale (VAS). A 3% absolute reduction

and 6.6% relative reduction from baseline were found for pain ( $P < 0.05$ ; SMD, 0.19; 95% CI, 0.04 to 0.35;  $n = 638$ ). No statistically significant differences were found for walking ability or stiffness.

Next, we examined the effectiveness of aquatic exercise for pain relief.<sup>2</sup> Aquatic exercise was significantly inversely associated with pain ( $P < 0.05$ ; SMD,  $-0.17$ ; 95% CI,  $-0.33$  to  $-0.01$ ;  $n = 594$ ). However, meta-analysis showed no differences between aquatic exercise and land exercise ( $P = 0.56$ ; SMD, 0.11; 95% CI,  $-0.27$  to 0.50;  $n = 103$ ).

We then examined the effectiveness of spa therapy (with physiotherapy) and balneotherapy for treating low back pain.<sup>16</sup> Pain was assessed using a 100-mm VAS. Spa therapy was significantly inversely associated with pain ( $P < 0.001$ ; SMD, 26.6; 95% CI, 20.4 to 32.8;  $n = 442$ ), as was balneotherapy ( $P < 0.001$ ; SMD, 18.8; 95% CI, 10.3 to 27.3;  $n = 138$ ). Results on the Schober index and assessment of lumbar flexibility suggested there were no significant intergroup differences.

### Withdrawals and adverse events

Withdrawals (dropouts) were reported in 3 studies, and adverse events were reported in 4 studies (Table 4). No fatal accidents or serious adverse effects were noted in studies that reported adverse events.

### Quality assessment

A list of excluded studies (3 trials, 43%) and the use of graphic aids to assess publication bias (1 trial, 14%) were evaluated by using the AMSTAR checklist (Table 5).

## DISCUSSION

We identified only 7 published SRs on aquatic exercise and balneotherapy, which indicates that there is little evidence demonstrating the effectiveness of the warmth, buoyancy, and

**Table 1. Summary of articles based on structured abstracts (aim and methods)**

No.	Author	Journal Year; Vol.; Page.	Title	Aim/Objective	Data source/Search strategy	Selection criteria/period of intervention	Data extraction/Data collection and analysis
1	Bartels EM, et al.	Cochrane Database Syst Rev 2007;4:CD005523. (in English)	Aquatic exercise for the treatment of knee and hip osteoarthritis.	To compare the effectiveness and safety of aquatic exercise interventions in the treatment of knee and hip osteoarthritis.	MEDLINE from 1949, EMBASE from 1980, CENTRAL (Issue 2, 2006), CINAHL from 1982, Web of Science from 1945, all up to May 2006. There was no language restriction.	Randomized controlled trials or quasi-randomized clinical trials. The duration of interventions was from 6 weeks to 12 months.	Two review authors independently selected trials for inclusion, assessed the internal validity of included trials and extracted data. Pooled results were analyzed using standardized mean differences (SMD).
13	Verhagen AP, et al.	Cochrane Database Syst Rev 2008;3:CD000518. (in English)	Balneotherapy for rheumatoid arthritis.	To assess the effectiveness of balneotherapy for rheumatoid arthritis.	They searched the following databases up to October 2006: CENTRAL (Issue 3, 2006), PubMed, CINAHL, the database from the Cochrane "Rehabilitation and Related Therapies" Field and Pedro, and performed reference checking and personal communications with authors to retrieve eligible studies.	Selection criteria: randomized controlled trials comparing balneotherapy with any other intervention or with no intervention. Included patients were all suffering from definite or classical rheumatoid arthritis as defined by the American Rheumatism Association Criteria or by the criteria of Steinbrocker. At least one of the WHO/ILAR core set of endpoints for RA clinical trials had to be among the main outcome measures. The duration of interventions was from 14 weeks to 6 months and 4 weeks.	Two authors independently assessed quality and extracted data. Disagreements were solved by consensus.
14	Verhagen AP, et al.	Cochrane Database Syst Rev 2007;4:CD006864. (in English)	Balneotherapy for osteoarthritis.	To assess the effectiveness of balneotherapy for patients with osteoarthritis (OA).	They searched the following databases up to October 2006: EMBASE, PubMed, the Cochrane "Rehabilitation and Related Therapies" Field database, PEDro, CENTRAL (Issue 3, 2006), and performed reference checking and communicated with authors to retrieve eligible studies.	Randomized controlled trials (RCT) comparing balneotherapy with any intervention or no intervention. At least 90% of the patient population had to be diagnosed with osteoarthritis; duration of interventions was from 15 days to 27 weeks.	Two authors independently assessed quality and extracted data. Disagreements were solved by consensus. In the event of clinical heterogeneity or lack of data they refrained from statistical pooling.

*Continued on next page.*



Continued.

No.	Author	Journal Year; Vol.; Page.	Title	Aim/Objective	Data source/Search strategy	Selection criteria/period of intervention	Data extraction/Data collection and analysis
15	Forestier R, et al.	Joint Bone Spine 2008;75:138–148. (in English)	Crenobalneotherapy for limb osteoarthritis: Systematic literature review and methodological analysis.	To conduct a systematic literature review on crenobalneotherapy for limb osteoarthritis and to discuss the study methods used to evaluate this treatment modality.	They searched the Medline database. They also reviewed the reference lists of articles retrieved by the Medline search. The studies had to be written in English or French.	Studies that compared crenobalneotherapy to other interventions or to no intervention were considered. Massage (usually an integral part of spa programs) is not specific to spa therapy and therefore was not studied here. Only studies of patients with osteoarthritis of the knee, hip, and/or hands were selected. The duration of interventions was from 16 days to 1 year and 3 months.	They used a checklist specifically designed to evaluate the internal validity of nonpharmacological trials. External validity and the quality of the statistical analysis were also evaluated.
16	Pittler MH, et al.	Rheumatol 2006;45:880–883. (in English)	Spa therapy and balneotherapy for treating low back pain: meta-analysis of randomized trials.	To assess the evidence for or against the effectiveness of spa therapy and balneotherapy for treating low back pain.	Systematic searches were conducted on Medline, Embase, Amed Cochrane Central, the UK National Research Register and ClinicalTrials.gov (all until July 2005).	All trials reporting that the sequence of allocation was randomized (RCTs). Testing balneotherapy or spa therapy for treating patients with low back pain were included. Trials reported in duplicate were excluded. The duration of interventions was from 3 weeks to 4 weeks.	Data abstraction was performed systematically and independently according to design, quality, sample size, intervention, water characteristics, results, adverse events and concomitant treatment.
2	Hall J, et al.	Arch Phys Med Rehabil 2008;89:873–883. (in English)	Does aquatic exercise relieve pain in adults with neurologic or musculoskeletal disease? A systematic review and meta-analysis of randomized controlled trials.	To evaluate the literature on the effectiveness of aquatic exercise in relieving pain in adults with neurologic or musculoskeletal disease.	A systematic literature search of 14 databases was examined for research on aquatic exercise over the period from January 1980 to June 2006.	Randomized controlled trials (RCTs) that included adults with neurologic or musculoskeletal disease, pain as an outcome measure, and exercise in water were included. The duration of interventions was from 4 weeks to 12 months.	Information on the participants, interventions, and outcomes was extracted from the included studies. Quality appraisal was assessed using the Scottish Intercollegiate Guidelines Network criteria for RCTs.
17	Kamioka H, et al.	J Jpn Soc Balneol Climatol Phys Med 2006;69:155–166. (in Japanese with English abstract)	A systematic review of randomized controlled trials on the therapeutic and health-promoting effects of spas.	To review randomized controlled trials of the effects of treatment in spas, thereby clarifying therapeutic effects of these treatments on individual diseases, and its health-promoting effects.	They searched the PubMed database twice: in Sept. 2004 and in April 2005. Articles published after 1990 and written in English were searched.	Key words for study selection were “randomized controlled trial” and “spa” or “balneotherapy”. No criteria were set up concerning the number of subjects, the observation period, or the kind of disease studied. The duration of interventions was from 3 weeks to 12 months.	The quality of individual articles was evaluated on a 13-point modified PEDro scale that was constructed by adding three terms, representing the number of subjects, the observation period, and water characteristics to the 10-point PEDro scale.

**Table 2. Summary of articles based on structured abstracts (results and conclusion)**

No.	Author	Main results	Conclusion
1	Bartels EM, et al.	In total, six trials (800 participants) were included. At the end of treatment for combined knee and hip osteoarthritis, there was a small-to-moderate effect on function (SMD 0.26, 95% confidence interval (CI) 0.11 to 0.42) and a small-to-moderate effect on quality of life (SMD 0.32, 95% CI 0.03 to 0.61). A minor effect of a 3% absolute reduction (0.6 fewer points on a 0 to 20 scale) and 6.6% relative reduction from baseline was found for pain. Only two studies reported adverse effects, that is, the interventions did not increase self-reported pain or symptom scores.	Aquatic exercise appears to have some beneficial short-term effects for patients with hip and/or knee OA; no long-term effects were documented. The controlled and randomized studies in this area are still too few to give further recommendations on how to apply the therapy, and studies of clearly defined patient groups with long-term outcomes are needed.
13	Verhagen AP, et al.	One extra study is included in this update. Now seven trials (412 patients) were included in this review. Most trials reported positive findings on their main outcomes, but were methodologically flawed to some extent. A 'quality of life' outcome was reported by two trials. None of the trials performed an intention-to-treat analysis and only two performed a comparison of effects between groups. Pooling of the data was not performed because of heterogeneity of the studies, multiple outcome measurements, and the overall poor data presentation. We found a significant benefit of mineral baths compared to Cyclosporine A at eight weeks on pain in one study (RR = 2.4; 95% CI: 1.4, 3.8). Overall there is insufficient evidence that balneotherapy is more effective than no treatment, that one type of bath is more effective than another, or that one type of bath is more effective than mudpacks, exercise, or relaxation therapy.	Silver level evidence was found for one study in favor of mineral baths compared to drug treatment at eight weeks. Insufficient evidence was found for all other comparisons. However the scientific evidence is insufficient because of poor methodological quality. Therefore, the noted "positive findings" should be viewed with caution.
14	Verhagen AP, et al.	Seven trials (498 patients) were included in this review. Two studies compared spa treatment with no treatment. One study evaluated baths as an add-on treatment to home exercise and the author compared thermal water from Cserkeszolo with tap water (placebo). Three studies compared sulphur or Dead Sea baths with no treatment or mineral baths with tap water baths or no treatment. Only one of the trials performed an intention-to-treat analysis and two studies provided enough data to perform our own intention-to-treat analysis. A 'quality of life' outcome was reported by one trial.	They found silver level evidence concerning the beneficial effects of mineral baths compared to no treatment. Regarding all other balneological treatments, no clear effects were found. However, the scientific evidence is weak because of the poor methodological quality and the absence of adequate statistical analysis and data presentation. The noted "positive findings" should be viewed with caution.
15	Forestier R, et al.	Crenobalneootherapy was associated with improvements in the evaluation criteria (pain, function, and quality of life) compared to baseline. However, inadequate internal validity precluded the establishment of a causal link between these improvements and crenobalneootherapy. External validity was often poorly defined. Some studies found no significant differences with the control group but failed to include a sample-size calculation, suggesting inadequate statistical power as a possible explanation for the result. In several studies, the use of multiple evaluation criteria and measurements led to a high risk of Type I error.	Although the consistency of the results suggests a therapeutic effect of crenobalneootherapy in limb osteoarthritis, available studies are methodologically inadequate and sample sizes too small to allow definitive conclusions. They suggest a number of solutions to these shortcomings. Carefully designed studies in larger patient populations are needed to determine the role of crenobalneootherapy in knee osteoarthritis.
16	Pittler MH, et al.	Five randomized clinical trials met all inclusion criteria. Quantitative data synthesis was performed. The data for spa therapy, assessed on a 100-mm visual analogue scale (VAS), suggest significant beneficial effects compared with waiting list control groups (weighted mean difference 26.6 mm, 95% confidence interval 20.4–32.8, $n = 442$ ) for patients with chronic low back pain. For balneotherapy, the data, assessed on a 100-mm VAS, also suggest beneficial effects compared with control groups (weighted mean difference 18.8 mm, 95% confidence interval 10.3–27.3, $n = 138$ ).	Even though the data are scarce, there is encouraging evidence suggesting that spa therapy and balneotherapy may be effective for treating patients with low back pain. These data are not compelling but warrant rigorous large-scale trials.
2	Hall J, et al.	Nineteen studies met the inclusion criteria; 8 had a moderate-to-low risk of bias, and 5 of these had data suitable for meta-analyses. This showed that aquatic exercise has a small posttreatment effect in relieving pain compared with no treatment ( $P = .04$ ; standardized mean difference [SMD], $-.17$ ; 95% confidence interval [CI], $-.33$ to $-.01$ ), but it is not possible to draw a firm conclusion because of the lack of consistency of evidence across studies. Comparable pain-relieving effects were found between aquatic and land-based exercise ( $P = .56$ ; SMD = $.11$ ; 95% CI, $-.27$ to $.50$ ).	There is sound evidence that there are no differences in pain-relieving effects between aquatic and land exercise. Compared with no treatment, aquatic exercise has a small pain-relieving effect; however, the small number of good-quality studies and inconsistency of results means that insufficient evidence limits firm conclusions.
17	Kamioka H, et al.	A total of 17 articles were reviewed. Diseases studied in these articles were mostly locomotor disorders, with pain as a main symptom: rheumatism, osteoarthritis, lumbago, Parkinson's disease, varicosis, psoriasis, and health-promotion. The mean score on the 13-point modified PEDro scale was 7.5 (SD, 2.3), with a minimum score of 2 points and a maximum score of 12 points. In addition to balneotherapy, exercise therapy, mud pack treatment, and douche massage were employed in numerous studies. Improvements in the indicators were always more marked in balneotherapy intervention groups than in control groups, irrespective of the disease studied.	They devised a "3-layer model of evidence to be accumulated in balneotherapy" and concluded that RCT quality, evidence level, and expectation of good results were high for, in descending order, pain-relieving effect, functional recovery and improvement in quality of life, and health-promoting effects.

**Table 3. Brief summary of 7 systematic reviews**

No.	Author	Year of publication	Intervention type	Meta-analysis	Object disease	Effects noted
1	Bartels EM, et al.	2007	Aquatic exercise	Performed	Hip and knee Osteoarthritis	Short-term effects
13	Verhagen AP, et al.	2008	Balneotherapy	Not performed	Rheumatoid arthritis	Unclear, but effects in some trials
14	Verhagen AP, et al.	2007	Balneotherapy	Not performed	Osteoarthritis	Unclear, but effects in some trials
15	Forestier R, et al.	2008	Balneotherapy	Not performed	Limb osteoarthritis	Unclear, but effects in some trials
16	Pittler MH, et al.	2006	Balneotherapy and aquatic exercise	Performed	Low back pain	Effect for both interventions
2	Hall J, et al.	2008	Aquatic exercise	Performed	Neurologic or musculoskeletal disease	Small effect
17	Kamioka H, et al.	2006	Balneotherapy	Not performed	Locomotor disease and health improvement	Unclear, but effects in some trials

**Table 4. Description of adverse events and withdrawals in articles**

No.	Author	Title	Withdrawals (dropouts) described?	Adverse events described?
1	Bartels EM, et al.	Aquatic exercise for the treatment of knee and hip osteoarthritis	Yes	Yes
14	Verhagen AP, et al.	Balneotherapy for rheumatoid arthritis	Yes	Yes
15	Verhagen AP, et al.	Balneotherapy for osteoarthritis	Yes	Yes
16	Forestier R, et al.	Crenobalneotherapy for limb osteoarthritis: Systematic literature review and methodological analysis	Yes	No
17	Pittler MH, et al.	Spa therapy and balneotherapy for treating low back pain: meta-analysis of randomized trials	No	Yes
2	Hall J, et al.	Does aquatic exercise relieve pain in adults with neurologic or musculoskeletal disease? A systematic review and meta-analysis of randomized controlled trials	Yes	Yes
18	Kamioka H, et al.	A systematic review of randomized controlled trials on the therapeutic and health-promoting effects of spas	No	No

hydrostatic effects of water for curing disease or improving health. One reason for the limited number of SRs may be that aquatic exercise and balneotherapy are similar practices and distinguishing between them in RCTs is thus difficult. In addition, participants may find the intervention process, which requires them to undress and wear a swimsuit, to be troublesome. Furthermore, it is difficult to perform meta-analyses because, in the case of balneotherapy, the chemical content and temperature of the waters studied differ in various countries and the data are therefore not easily integrated.

#### **Aquatic exercise versus balneotherapy (without exercise)**

We distinguished between aquatic exercise and balneotherapy to determine which was more effective, because many studies do not do so. Aquatic exercise had a small but statistically significant effect on pain, function, QOL and mental health, and included more voluntary movements

during water immersion. This suggests that an intervention requiring exercise is more effective for the treatment of musculoskeletal diseases, as compared to balneotherapy, which involves passive immersion. However, it should be noted that this was only the immediate effect of intervention, and not the long-term result. The intervention period ranged from 3 weeks to 12 months in aquatic exercise studies, and from 15 days to 12 months in studies of balneotherapy. This might reflect the difficulty of maintaining long-term participation in an RCT. Whatever the case, the long-term effects are not clear.

We did not pool data from SRs of balneotherapy<sup>13-15,17</sup> because of their heterogeneity, multiple and varied outcome measurements, and poor overall quality. SRs of balneotherapy suggested that the scientific evidence was insufficient because of the poor methodological quality of RCTs of balneotherapy. Thus, it is difficult to determine the independent effect of balneotherapy without exercise.

**Table 5. Evaluation of the quality of systematic reviews by using the AMSTAR checklist<sup>11</sup>**

No.	Items	Answer	<i>n</i>	(%)
1.	Was an 'a priori' design provided? The research question and inclusion criteria should be established before the conduct of the review.	Yes	7	(100)
		No	0	(0)
		Can't answer	0	(0)
		Not applicable	0	(0)
2.	Was there duplicate study selection and data extraction? There should be at least two independent data extractors and a consensus procedure for disagreements should be in place.	Yes	6	(86)
		No	0	(0)
		Can't answer	1	(14)
		Not applicable	0	(0)
3.	Was a comprehensive literature search performed? At least two electronic sources should be searched. The report must include years and databases used (e.g., Central, EMBASE, and MEDLINE). Key words and/or MESH terms must be stated and where feasible the search strategy should be provided. All searches should be supplemented by consulting current contents, reviews, textbooks, specialized registers, or experts in the particular field of study, and by reviewing the references in the studies found.	Yes	5	(71)
		No	2	(29)
		Can't answer	0	(0)
		Not applicable	0	(0)
4.	Was the status of publication (i.e., grey literature) used as an inclusion criterion? The authors should state that they searched for reports regardless of their publication type. The authors should state whether or not they excluded any reports (from the systematic review), based on their publication status, language etc.	Yes	7	(100)
		No	0	(0)
		Can't answer	0	(0)
		Not applicable	0	(0)
5.	Was a list of studies (included and excluded) provided? A list of included and excluded studies should be provided.	Yes	3	(43)
		No	4	(57)
		Can't answer	0	(0)
		Not applicable	0	(0)
6.	Were the characteristics of the included studies provided? In an aggregated form such as a table, data from the original studies should be provided on the participants, interventions and outcomes. The ranges of characteristics in all the studies analyzed e.g., age, race, sex, relevant socioeconomic data, disease status, duration, severity, or other diseases should be reported.	Yes	7	(100)
		No	0	(0)
		Can't answer	0	(0)
		Not applicable	0	(0)
7.	Was the scientific quality of the included studies assessed and documented? 'A priori' methods of assessment should be provided (e.g., for effectiveness studies if the author(s) chose to include only randomized, double-blind, placebo controlled studies, or allocation concealment as inclusion criteria); for other types of studies alternative items will be relevant.	Yes	7	(100)
		No	0	(0)
		Can't answer	0	(0)
		Not applicable	0	(0)
8.	Was the scientific quality of the included studies used appropriately in formulating conclusions? The results of the methodological rigor and scientific quality should be considered in the analysis and the conclusions of the review, and explicitly stated in formulating recommendations.	Yes	7	(100)
		No	0	(0)
		Can't answer	0	(0)
		Not applicable	0	(0)
9.	Were the methods used to combine the findings of studies appropriate? For the pooled results, a test should be done to ensure the studies were combinable, to assess their homogeneity (i.e. Chi-squared test for homogeneity). If heterogeneity exists a random effects model should be used and/or the clinical appropriateness of combining should be taken into consideration (i.e., is it sensible to combine?).	Yes	5	(71)
		No	1	(14)
		Can't answer	1	(14)
		Not applicable	0	(0)
10.	Was the likelihood of publication bias assessed? An assessment of publication bias should include a combination of graphical aids (e.g., funnel plot, other available tests) and/or statistical tests (e.g., Egger regression test).	Yes	1	(14)
		No	6	(86)
		Can't answer	0	(0)
		Not applicable	0	(0)
11.	Was the conflict of interest stated? Potential sources of support should be clearly acknowledged in both the systematic review and the included studies.	Yes	5	(71)
		No	2	(29)
		Can't answer	0	(0)
		Not applicable	0	(0)

**Table 6. Overall evidence and future research agenda**

Intervention	Evidence	Specific agenda	Common agenda
Aquatic exercise	Small but significant effect (no differences between aquatic exercise and land exercise)	1. Long-term effect 2. Type of dose (intensity, frequency and duration)	1. Randomized controlled trials for various diseases 2. Cost-benefit analysis 3. Description of adverse effects
Balneotherapy	Poor/Unclear	Satisfactory methodology (intention-to-treat analysis, blinding, adequate control group, etc.)	

### Quality assessment

Seven of the included SRs were published after 2006 and, hence, relatively recent. We used the AMSTAR checklist because its content validity is high and the number of articles reviewed to evaluate SR quality was as few as 11. The requirements of the AMSTAR checklist were generally satisfied; however, an assessment of publication bias was frequently omitted. The AMSTAR requires that an assessment of publication bias include a combination of graphic aids (eg, funnel plot other available tests). One important publication reported that authors were more likely to publish RCTs in an English-language journal if the results were statistically significant.<sup>18</sup> English language bias may therefore be present in reviews and meta-analyses that include only trials reported in English.

There were few lists of excluded studies: only 3 Cochrane Reviews<sup>1,13,14</sup> reported this information. If the format of SRs adheres to that of the Cochrane Review, recording omissions would be minimal. However, many scientific journals limit the length of submissions, so such descriptions may not be published. We believe it is necessary to include a list of excluded studies in order to improve the certainty and transparency of studies.

### Overall evidence and future research agenda

Table 6 shows the overall evidence and future research agenda for aquatic exercise and balneotherapy. Aquatic exercise had a small but statistically significant effect. Future RCTs should investigate the long-term effectiveness of aquatic exercise or its effectiveness with respect to type or duration of exercise. Then, SRs based on such RCTs can be conducted. Regarding balneotherapy, RCTs based on appropriate research methodology are needed because no clear effect was found in the present study. A common problem with RCTs is that they do not properly evaluate adverse effects; future studies should include these data.

A recent study suggested that the most important questions that authors of systematic reviews face are as follows<sup>19</sup>: (1) How can incorporating existing reviews into new work adhere to the principles of comprehensive, transparent, and unbiased methods required for systematic reviews? (2) If an effort is made to incorporate existing reviews, will it save time and resources? (3) Are there instances where an independent, critical assessment of the evidence warrants conducting a

complex review “from scratch” even if there are existing reviews?

### Study limitations

There were several limitations to the present study. Some selection criteria were common to the studies, as described above; however, bias remained due to differences in the eligibility for participation in each study.

Publication bias was also a limitation. Although we did not limit our search to English language articles, we found no articles published in other languages. Also, we were not able to check references by means of hand searches. Nor were we able to contact institutions, societies, or specialists with expertise in aquatic exercise or balneotherapy or authors of included studies to identify any additional published or unpublished data. Another limit of the study was that we were not able to search the PEDro database, which is used in fields such as rehabilitation medicine and physiotherapy.

In terms of quality assessment, disagreements and uncertainties were resolved by discussion between 2 authors; discussions with a third expert and contact with authors for the purpose of clarification were not allowed.

### Conclusion

There were relatively few SRs of RCTs on aquatic exercise and balneotherapy. We found that aquatic exercise had a small but statistically significant effect on pain relief and related outcome measurements for locomotor diseases. However, the long-term effectiveness of these treatments remains unclear.

Because there was insufficient evidence due to the poor methodological quality of balneotherapy studies, we are unable offer any conclusions about the effects of this intervention. Common flaws included an inadequate description of excluded RCTs and insufficient assessment of publication bias.

### ACKNOWLEDGEMENTS

This study was supported by Health and Labour Sciences Research Grants (Research on Health Security Control: ID No. H20-007) from the Japanese Ministry of Health, Labour and Welfare in 2008. We would like to express our appreciation to M. Makishi, Y. Yamada, and S. Moriyama for their assistance in this study.

**Appendix. Studies excluded in the present review**

No.	Author. Journal (Year)	Title	Reason for exclusion
E1	Cardoso JR, et al. Cochrane Database Syst Rev (2008)	Aquatic therapy exercise for treating rheumatoid arthritis (Protocol)	Not reviewed due to protocol
E2	Beamon S, et al. Cochrane Database Syst Rev (2008)	Hydrotherapy for asthma (Protocol)	Not reviewed due to protocol
E3	Dziedzic K, et al. Best Practice Research Clin Rheumatol (2008)	Land- and water-based exercise therapies for musculoskeletal condition	Not SR
E4	Getz M, et al. Clin Rehabil (2006)	Effects of aquatic interventions in children with neuromotor impairments: a systematic review of the literature	Not SR based on RCTs
E5	Tejirian T, et al. Diseases Colon Rectum (2005)	Sitz bath: where is the evidence? Scientific basis of a common practice	Not SR
E6	Herman PM, et al. BMC Complementary Alternative Med (2005)	Is complementary and alternative medicine (CAM) cost-effective? a systematic review	Not SR based on water
E7	Karagulle MZ, et al. Forsch Komplementarmed Klass Naturheilkd (2004)	Balneotherapy and spa therapy of rheumatic diseases in Turkey: a systematic review (in German)	Not SR based on RCTs
E8	Meremikwu M, et al. Cochrane Database Syst Rev (2008)	Physical methods for treating fever in children	Not SR based on water
E9	Liao WC. Int J Nursing Studies (2002)	Effects of passive body heating on body temperature and sleep regulation in the elderly: a systematic review	Not SR based on RCTs
E10	Pennick VE, et al. Cochrane Database Syst Rev (2007)	Interventions for preventing and treating pelvic and back pain in pregnancy	Not SR based on water
E11	Teschendorf ME, et al. Am J Maternal/Child Nursing (2000)	Hydrotherapy during labor: an example of developing a practice policy	Not SR based on RCTs
E12	Verhagen AP, et al. J Rheumatol (1997)	Taking baths: the efficacy of balneotherapy in patients with arthritis. A systematic review	Not SR based on RCTs
E13	Sim J, et al. Clin J Pain (2002)	Systematic review of randomized controlled trials of nonpharmacological interventions for fibromyalgia	Not SR based on water
E14	Rosimini C, et al. J Am Academy Nurse Practitioners (2003)	Benefits of swim training for children and adolescents with asthma	Not SR based on RCTs
E15	Schiltewolf M, et al. Schmerz (2008)	Physiotherapy, exercise and strength training and physical therapies in the treatment of fibromyalgia syndrome (in German)	Not SR based on RCTs
E16	Toumaire M, et al. e CAM (2007)	Complementary and alternative approaches to pain relief during labor	Not SR
E17	Bouchama A, et al. Critical Care (2007)	Cooling and hemodynamic management in heatstroke: practical recommendations	Not SR based on RCTs
E18	Iarustovskaia OV, et al. Vopr Kurotol Fizioter Lech Fiz Kult (2006)	Thermocontrast hydrotherapy in the treatment of neuroendocrine disorders in females of reproductive age (in Russian)	Not SR based on RCTs
E19	Balint G, et al. Orv Hetil (2006)	Rehabilitation and balneotherapy, wellness 2004 (in Hungarian)	Not SR based on RCTs
E20	Adilov VB, et al. Vopr Kurotol Fizioter Lech Fiz Kult (2006)	Mineral waters for external (balneological) application. Guide for physicians (in Russian)	Not SR
E21	Markel W. Wien Klin Wochenschr (2006)	Can the effects of radon therapy be scientifically substantiated? (in Russian)	Not SR
E22	Getenbrunner C. Wien Klin Wochenschr (2006)	Could balneology and medical climatology have more than historic importance in the therapy of chronic diseases? (in Russian)	Not SR
E23	Davydova DB, et al. Vopr Kurotol Fizioter Lech Fiz Kult (2006)	Hydrobalneotherapy of patients with cardiovascular disease. Manual for physicians (in Russian)	Not SR
E24	Hodgson S. Clin Orthopaedics Related Research (2006)	Proximal humerus fracture rehabilitation	Not SR based on RCTs
E25	Liu Y, et al. Current Opinion Rheumatol (2004)	Recent advances in the treatment of the spondyloarthropathies	Not SR based on water
E26	Watts R, et al. Int J Nursing Practice (2003)	Nursing management of fever in children: a systematic review	Not SR based on water
E27	Pengel HM, et al. Clin Rehabil (2002)	Systematic review of conservative interventions for subacute low back pain	Not SR based on water
E28	Constant F, et al. Bull Soc Sci Med Grand Duche Luxemb (1995)	Critical bibliographic analysis of international medical literature in the domain of thermal research	Not SR based on RCTs

## REFERENCES

1. Bartels EM, Lund H, Hagen KB, Dagfinrud H, Christensen R, Danneskiold-Samsøe B. Aquatic exercise for the treatment of knee and hip osteoarthritis. *Cochrane Database Syst Rev.* 2007;(4):CD005523.
2. Hall J, Swinkels A, Briddon J, McCabe CS. Does aquatic exercise relieve pain in adults with neurologic or musculoskeletal disease? A systematic review and meta-analysis of randomized controlled trials. *Arch Phys Med Rehabil.* 2008;89:873–83.
3. Bender T, Karagülle Z, Bálint GP, Gutenbrunner C, Bálint PV, Sukenik S. Hydrotherapy, balneotherapy, and spa treatment in pain management. *Rheumatol Int.* 2005;25:220–4.
4. Yamazaki F, Endo Y, Torii R, Sagawa S, Shiraki K. Continuous monitoring of change in hemodilution during water immersion in humans: effect of water temperature. *Aviat Space Environ Med.* 2000;71:632–9.
5. Gabrielsen A, Videbaek R, Johansen LB, Warberg J, Christensen NJ, Pump B, et al. Forearm vascular and neuroendocrine responses to graded water immersion in humans. *Acta Physiologica Scand.* 2000;169:87–94.
6. Fam AG. Spa treatment in arthritis: a rheumatologist's view. *J Rheumatol.* 1991;18:1775–7.
7. Nguyen M, Revel M, Dougados M. Prolonged effects of 3 week therapy in a spa resort on lumbar spine, knee and hip osteoarthritis: follow-up after 6 months. A randomized controlled trial. *Br J Rheumatol.* 1997;36:77–81.
8. Franke A, Reiner L, Pratzel HG, Frank T, Resch KL. Long-term efficacy of radon spa therapy in rheumatoid arthritis: A randomized, sham-controlled study and follow-up. *Rheumatology.* 2000;39:894–902.
9. Kamioka H, Nakamura Y, Yazaki T, Uebaba K, Mutoh Y, Okada S, et al. Effectiveness of comprehensive health education combining hot spa bathing and lifestyle education in middle-aged and elderly women: one-year follow-up on randomized controlled trial of three- and six-month interventions. *J Epidemiol.* 2006;16:35–44.
10. Kamioka H, Ohshiro H, Mutoh Y, Honda T, Okada S, Takahashi M, et al. Effect of long-term comprehensive health education on the elderly in a Japanese village: Unnan cohort study. *Int J Sports Health Sci.* 2008;6:1–6.
11. Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. *BMC Medical Research Methodology* [Internet] 2007 February 15[cited 2008 Dec 12]; 7(10):1–7. Available from: <http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1810543>.
12. Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, et al. Grading quality of evidence and strength of recommendations. *BMJ.* 2004;328:1490–7.
13. Verhagen AP, Bierma-Zeinstra SM, Boers M, Cardoso JR, Lameck J, de Bie RA. Balneotherapy for rheumatoid arthritis. *Cochrane Database Syst Rev.* 2004;(1):CD000518.
14. Verhagen AP, Bierma-Zeinstra SM, Boers M, Cardoso JR, Lambeck J, de Bie RA, et al. Balneotherapy for osteoarthritis. *Cochrane Database Syst Rev.* 2007;(4):CD006864.
15. Forestier R, Françon A. Crenobalneo-therapy for limb osteoarthritis: Systematic literature review and methodological analysis. *Joint Bone Spine.* 2008;75:138–48.
16. Pittler MH, Karagülle MZ, Karagülle M, Ernst E. Spa therapy and balneotherapy for treating low back pain: meta-analysis of randomized trials. *Rheumatology.* 2006;45:880–4.
17. Kamioka H, Kuroyanagi R, Komatsu T, Kaminai T, Takahashi M, Mutoh Y, et al. A systematic review of randomized controlled trials on the therapeutic and health-promoting effects of spas. *J Jpn Soc Balneol Climatol Phys Med.* 2006;69:155–66 (in Japanese with English abstract).
18. Egger M, Zellweger-Zähner T, Schneider M, Junker C, Lengeler C, Antes G. Language bias in randomized controlled trials published in English and German. *Lancet.* 1997;350:326–9.
19. Whitlock EP, Lin JS, Chou R, Shekelle P, Robinson KA. Using existing systematic reviews in complex systematic reviews. *Ann Intern Med.* 2008;148:776–82.

## くすりはリスク: 漢方薬から西洋薬をみる

津谷 喜一郎\*

## 1. くすりはリスク

東京医科歯科大学名誉教授でわたしの恩師である佐久間昭先生の『薬の効果・逆効果』(1981)という本の中に「くすり」の逆は「リスク」(危険)である」というフレーズが出てくる。図1に示す。「くすりにはリスクもあるよ」ということだ。この「くすりはリスク」は1980年代以降、日本で医療関係者にそれなりに広く使われた言葉である。

この本には医薬品を取り巻く社会的な要因に関しても触れられている。例えば、薬の商品としての特徴は「顧客能力が低い」、最近では「情報の非対称性」とも言われる。くすりは社会的な要因が大きい。これは現在もなくならない薬害問題にも関係する。

さらに歴史をたどると、1967年に『薬毒論』という本が、伊沢凡人編で出ている。田村豊幸、辰野高司、川瀬清を含め、4人で書かれている。図2に示す。この中には「薬禍現象出現のサイクル」として、薬のマーケットメカニズムのことも書かれている。この中に「新薬禍が生んだ漢方薬ブーム」という言葉が出てくる。

新薬に対する不安感、不信感があり、自然なもの、ナチュラルなものがよりよい、また安全と思っている人は多いものだ。わたしにもそういう傾向があった。

## 2. 伝統薬の多様性

「漢方薬」は人によって受け取り方がだいぶ異なる。わたしは1979年に医学部を卒業し北里研

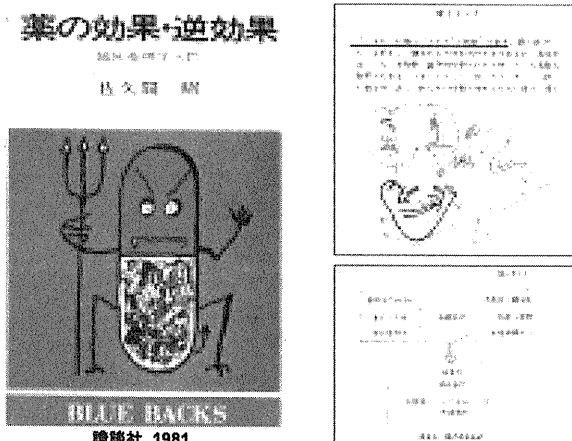


図1 「くすりはリスク」(1981)

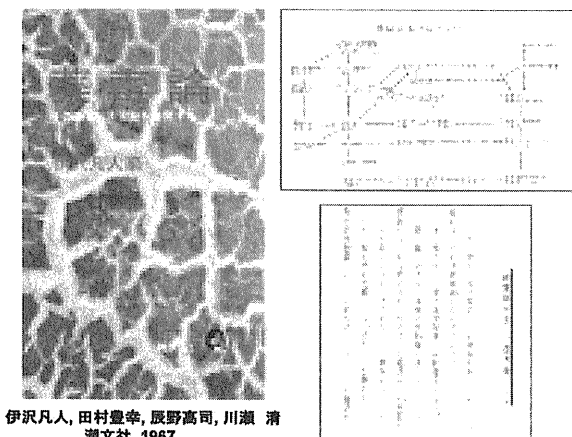


図2 『薬毒論』(1967)

究所付属東洋医学総合研究所に勤務し漢方と内科学を研修した。その後母校の難治疾患研究所臨床薬理学で佐久間先生のもとで学位を得、1984年か

\* 東京大学大学院薬学系研究科医薬政策学 〒113-0033 東京都文京区本郷 7-3-1





図3 元中国衛生部長・銭信忠 (Qian Xinzong), 1987

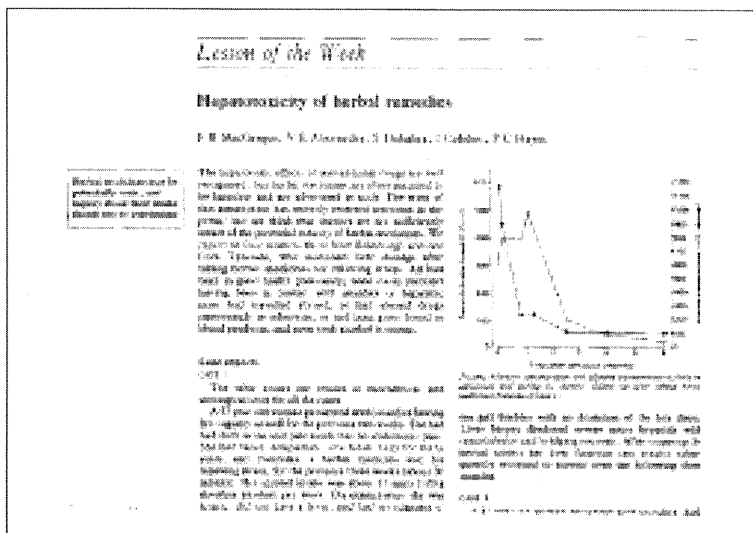


図4 BMJに収載されていた黄芩類似植物による肝機能障害の報告 (BMJ 1989 ; 299 (6708) : 1156-7)

らフィリピンのマニラにある WHO 西太平洋地域事務局に、初代の伝統医学担当医官として勤務した。

36 国・エリアを担当し、各国の現状調査にはじまり、政策立案、研究、教育、情報交換のプロジェクトをそれぞれ複数作成しモニタリングを行った。

そこで明らかになったのは伝統医学と伝統薬の多様性だ。パプアニューギニアの呪術医 witch が用いる薬草の粉、それらは文字化されていない。ラオスのお坊さんが用いる植物の葉にパーリ語で書いてある医学書中の薬草、ベトナムで中国系の医学の中で使われる処方、中国の政治的色彩が強い中で中西医結合の方針の中で使われる方剤、など。図3に写っているのは中国の元衛生部長（厚生大臣）・銭信忠先生で、中国で文化大革命時、「はだしの医者」という制度があったが、彼はモスクワ留学組で、中国人民のための医療の中心人物であった。そこでは政治と政策が大きな意味を持つ。

### 3. 1971 年代の WHO の政策の変化 —国際医薬品モニタリングと PHC—

国際医薬品モニタリング (International Drug Monitoring) のシステムは、もともと、サリドマイド事件の後、WHO が米国 FDA と協力してワ

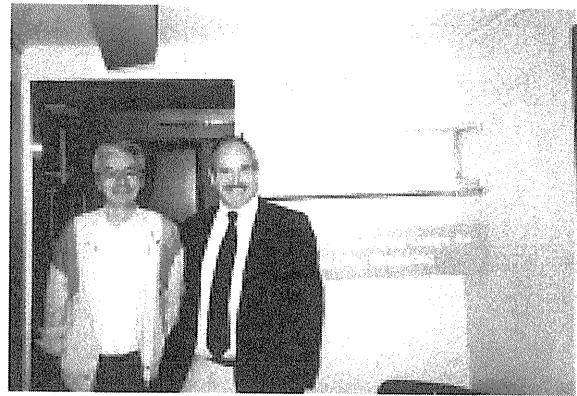
シントン DC の近くのアーリントンでパイロットプロジェクトとして始まったものだ。それがうまくいき、1968 年から WHO 本部のジュネーブで国際医薬品モニタリングのプログラムとして正式に活動が始まった。しかし先の中国の「はだしの医者」の影響もあって、国際保健では 1970 年代は世界的にプライマリーヘルスケア (PHC) が主流となった。1978 年にはアルマ・アータ宣言が出された。この国際医薬品モニタリングのプログラムには 20 人近いスタッフがいたが、PHC の政策の中で、国際医薬品モニタリングで副作用情報を集めることができるのは先進国しかない、必須医薬品 (essential drug) すら十分にいきわたっていない途上国を対象とした PHC にもっとお金を使うべきだ、とされ、予算がつかないことになった。それをスウェーデン政府が引きつぎ、ウプサラに拠点が移った。

### 4. 英国からの黄芩類似生薬の 副作用報告との出会い

わたしの WHO での勤務は、1 年の 1/3 が途上国への出張で、マニラでは管理的な仕事をしてきた。事務局では、いくつかの世界的な雑誌の回覧システムがあった。図4は 1989 年の *British Medical Journal* で “Hepatotoxicity of herbal



図5 中薬大辞典 (下冊, 1977, p. 2017-9) 記載の黄芩



WHO Collaborating Centre for International Drug Monitoring, Uppsala, 16 July 1995

図6 ウプサラの国際医薬品モニタリングセンター (1995)

remedies” という論文だ。わたしはもともと臨床薬理学で学位を得て、有効性と安全性に関心があり、生薬や漢方薬、英語では広く herbal medicines と称するが、その安全性を世界的な枠組みで考え始めたのはこの論文がきっかけだ。

読むと、*Scutellaria species* と書いてある。中国の江蘇新医学院編の『中薬大辞典』(1977)で探すと、全く同じ種ではないのだが、属が同じで黄芩類似植物がある。図5に示す。黄芩であれば、わたしは漢方をやっていたのですぐ分かる。洋の東西を問わず、この属には肝毒性があるらしいということが分かった。

### 5. Herbal medicines の安全性のシステムとしての捉え方

一昨年 2007 年に元筑波大学の内藤裕史先生が『健康食品・中毒百科』<sup>1)</sup>という優れた本を書かれた。彼は、日本の臨床薬理学の初期、1970年代から活躍されていた方だ。ここで健康食品は食品だけでなく生薬や漢方薬も含んでいる。これらは連続したスペクトルに位置するものだ。その序文にこう書いてある。「個々の事例という点と点を結ぶ細い糸を探し出し、その糸をたぐって布を織り、織りなす綾を読み取って鳥瞰図のようなものがで

ければ、被害を未然に防ぐ仕組みもできるし、未知の健康被害が発生したときの対応も容易である」。点—糸—布—綾—鳥瞰図という流れだ。たいへんよくできた考え方だ。一方で、個人の努力で綾を読んで鳥瞰図をつくるというのはやや無理があり、システム的な対応、とくに国際的な対応という視点が欠けているのではないかと思った。

わたしは 1990 年まで WHO で勤務し、その後 1 年ボストンで研究のまとめを行い、1991 年に日本に戻った。ICH の M1 トピックは医薬品行政用語集 (MedDRA) だ。わたしは 1995 年から 98 年まで、当時の厚生省から頼まれて ICH-M1 の厚生省側のトピックリーダーをしていた。当時は、WHO 副作用用語集 (WHO Adverse Reaction Terminology : WHO-ART) がまだ使われていた頃だ。それがひとつのソースにもなって MedDRA が作成されたわけだ。

図6は WHO-ART を用いた国際医薬品モニタリングとはどんなものかということで、1995年に ICH-M1 の日本人のチームでウプサラを訪ねた時のものだ。ここに写っているのが本日の午後特別講演をする Ralph Edwards 先生だ。当時はまだ Uppsala Monitoring Centre という言い方はなく、WHO International Drug Monitoring Centre と称していた。その後、政府からの財政支援がなくなり、名称が Uppsala Monitoring Centre (UMC) となった。

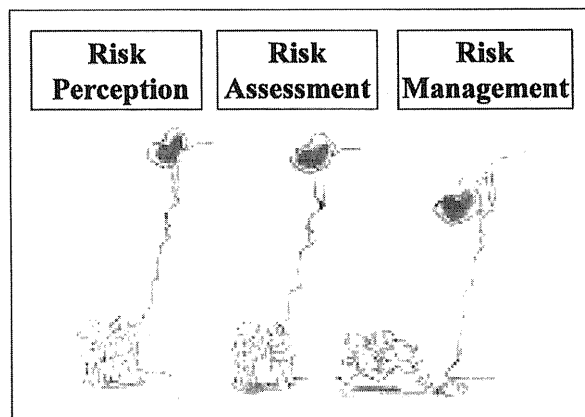


図7 リスク認知・リスク評価・リスク管理

ここでデータベースを担当している女性スタッフに「日本からどんな ADR レポートが入っているのか見せてくれ」と頼んだところ最初に出てきたのがなんと SAIKOKKEISHITO だ。わたしにはすぐに柴胡桂枝湯と分かった。しかし、これは日本語を読める日本人にしか分からない。なぜこれが最初に出るのかと聞くと「漢方薬は名前が明確でなくコードがないから入力が遅くなり、その結果先に出る」とのことであった。この1995年当時、広い意味での herbal medicines の副作用の報告が、世界から6,000件集まっていた。

### 6. 日本の小柴胡湯の副作用

1995年にウプサラを訪ねたことがきっかけで、WHO勤務時にBMJで読んだことを思い出し、洋の東西にまたがる herbal medicines の副作用についてきちんと論文にしないといけないと考え、1996年に共著論文を公表した<sup>2)</sup>。

図7に、リスク認知、リスク評価、リスク管理、の3段階を示す。1996年の論文は、時に引用されるが、行政にはあまりインパクトを与えなかった。リスク管理に役立たなかったことになる。同じ1996年3月2日の朝日新聞に、小柴胡湯の副作用で10人亡くなったという記事がでた。図8に示す。緊急安全性情報が出され、かなり大きなインパクトを与えた。漢方薬は「長年使ってきて安全性は保証されている」という神話が崩れかけた事件となった。



図8 小柴胡湯で10人死亡の記事 (1996.3.2)

その事件を契機に日本の漢方薬の使用パターンが大きく変わった。表1に1992年、1999年、2004年の使用パターンを示す。マーケットの約1/3を占めた小柴胡湯は大きく減少し、補中益気湯などの「補剤」が主要なウェイトを占めるようになった。この図は、医薬品の流れからいうと「川上」の生産動態統計を用い価格を metric とした医薬品使用実態調査 (drug utilization research : DUR) ともいえるものだ。

なお、医療用漢方製剤は1970年代に変則的な承認と保険給付の決定がなされたところから、常に保険外しの危機にさらされている。先週(2009年)11月3日に民主党政権による「事業仕分け」があった。OTCで類似薬がある場合には保険から外すべきという意見が出され、医療用漢方製剤も対象になり、それに対して反対運動が起きた。この時には、医療用漢方製剤すべてをまとめた議論がなされた。いくつかの分類、あるいは薬事行政という「クラス」に分けた議論も今後、必要かもしれない。補中益気湯はよい薬だが「補剤」のクラスにはいる。クラスごとの臨床的エビデンス、またエフェクトサイズ、さらに薬剤経済学的評価も必要だろう。

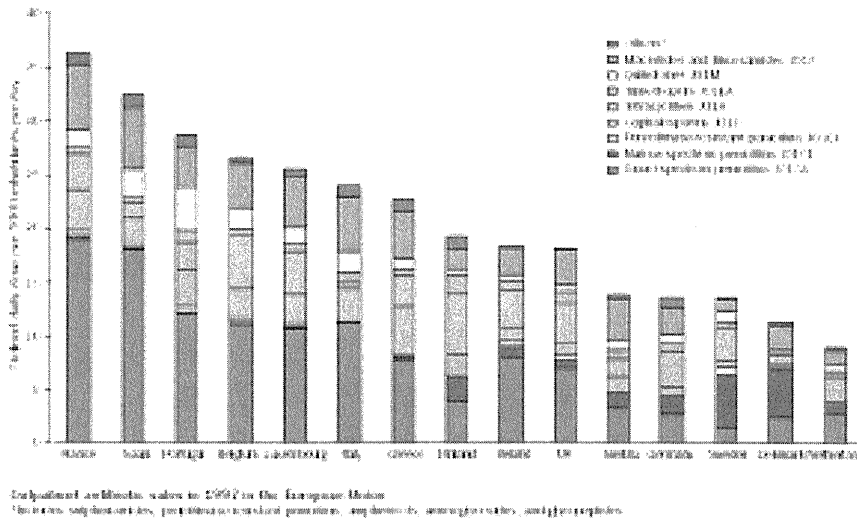
### 7. DURのためのATC/DDD

先に、使用パターンを示したが、そこでのDUR

表 1 1992 年, 1999 年, 2004 年の漢方薬の使用パターン

1992 年		1999 年		2004 年	
小柴胡湯	36.0%	小柴胡湯	10.2%	補中益気湯	6.9%
柴朴湯	4.9%	補中益気湯	6.2%	大建中湯	5.5%
補中益気湯	4.9%	柴苓湯	5.9%	柴苓湯	4.9%
八味地黄丸	3.3%	加味逍遙散	3.2%	加味逍遙散	3.8%
加味逍遙散	3.2%	大建中湯	3.0%	小柴胡湯	3.3%
六君子湯	2.7%	麦門冬湯	3.0%	麦門冬湯	3.0%
小青竜湯	2.4%	小青竜湯	2.3%	牛車腎気丸	3.0%
柴胡桂枝湯	2.4%	牛車腎気丸	2.2%	六君子湯	2.7%
大柴胡湯	2.3%	当帰芍薬散	2.1%	当帰芍薬散	2.4%
当帰芍薬散	2.1%	葛根湯	2.1%	小青竜湯	2.4%
その他	35.7%	その他	59.9%	その他	61.9%

「薬事工業生産動態統計年報」より著者が作成



Cars O, et al. Variation in antibiotic use in the European Union. *Lancet* 2001; 357: 1851-3

図 9 ATC/DDD を用いた抗生物質の drug utilization research (DUR)

で用いた「価格」は metric としての妥当性は高くない。価格は日本では薬価として 2 年に一度改正され、また各国で異なるため国際間比較ができない。

こうした理由から開発されたのが Defined Daily Dose (DDD) の考え方だ。図 9 にその代表的な使用例を示す。これはヨーロッパ各国の抗生物質の DUR で、縦軸は” Defined Daily Dose per 1,000 inhabitants per day ”となっている。つまり「1 日、住民 1,000 人あたり、何 DDD 使った

か？」をみるものだ。これを見るとフランスはオランダの 3.5 倍抗生物質を使用していると分かる。これに基づきフランス政府は医師に対する抗生物質の正しい使い方の教育を始めることになる。DDD を用いるとより正しく政策決定に用いることができる。

この DDD を求めるにはまず、医薬品の分類とコード化がなされていなければならない。そこで用いられているのが Anatomical, Therapeutic, and Chemical (ATC) Classification だ。図 10 に