Developing an integrative medicine patient care protocol from the existing practice of Ayurveda dermatology

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Doctors who use biomedicine with complementary and alternative medicine (CAM) in a carefully integrated way offer benefits from both systems to chronic patients without compromising on safety. The Institute of Applied Dermatology, Kasaragod has successfully developed a model of integrative medicine (IM) and effectively managed lymphoedema patients. This article describes the process of developing IM treatment adopting 'standard protocol items and recommendations for interventional trials'. All patients were examined by a team of doctors, biomedical and CAM, and nurses, thus enabling each patient's condition to be understood from these different perspectives, and diagnosis and management through an IM approach. A minimum of 30 min counselling is essential for every patient before informed consent is gained. The 'systems-based' conclusive process follows the standard guidelines in each therapeutic discipline. IM management is achieved following 'bedside discussion'. The minimum requirements for a clinical setting to conduct IM studies, documentation, patient selection and follow-up are described, utilizing biomedical outcome measures to demonstrate the effectiveness of IM. Components of the IM case record algorithm are described here. The process of clinical examination for Ayurveda is described along with comparative biomedical explanation. Biomedical confirmatory study, maintaining records of primary outcome measures, transcription of IM discussions and follow-up entries of patients under IM are also explained. Improving IM protocols for patient care has involved input from global experts together with feedback from patients who have received IM treatment. The IM treatment protocol should evolve as a patient-oriented approach. The protocol discussed here focuses on biomedical systems and structures to measure its effectiveness. This article provides a method for conducting evidence-based clinical studies to develop new IM therapies for chronic skin diseases.

Keywords: Integrative medicine, lymphoedema, patient care protocol, skin diseases.

Introduction

THE *British Medical Journal* has defined integrative medicine (IM) as giving prescriptions to patients, including drugs of both biomedicine, and complementary and alternative medicine (CAM), based on a biomedical diagnosis[1]. A Multi System Medical Team (MSMT) using a protocol developed for each disease[2] should manage patients receiving IM. Vaqas and Ryan[3] suggested that for the management of lymphoedema, the integration of Ayurveda, Yoga and biomedicine might be a possible way forward. Several publications describe the integration of CAM with biomedicine, albeit with a low number of patients, and minimum details on how they used medicines. Such studies rely heavily on 'pragmatic' trials[4]. Some lack an algorithm or internationally accepted protocol items for replication[5]. Clinicians and support staff in the treatment team should provide protocol-based IM patient care. Health care team should document the clinical features and treatment methods at all stages from a patients' entry to study until discharge from treatment. The available literature lack information on the process of conducting IM studies and general guidelines on reporting them.

IM treatments are developed using prospective studies where one or more interventions from biomedicine and CAM are administered to patients and their effects on health-related outcomes are assessed. Unfortunately, this often leads to problems with confounding factors. Most papers using IM or CAM in trials describe diseases where mechanisms of causation and targets are not clearly understood. This requires in-depth reviews of existing treatment strategies in CAM. Such papers are mostly written by two or more authors who belong to entirely different disciplines of science – modern and traditional. Due to the frequently unstructured patient care in CAM, most studies must follow an observational design, creating a significant barrier to reporting them in the clear style of biomedical journals.

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Over the last decade, the Institute of Applied Dermatology (IAD), Kasaragod has developed an IM protocol for managing lower-limb lymphoedema[6]. Proven biomedical outcome measures were used to show the effectiveness of this treatment template. Thus, a paradigm of IM for dermatology evolved, as the result of a patient-oriented clinical research led by a MSMT at IAD[2].

This article describes the paradigm of IM for dermatology to develop new patient care protocols for chronic and difficult-to-manage skin diseases by combining Ayurveda, Yoga and biomedical drugs. To improve the quality of IM protocols, and facilitate proper conduct, transparent and complete reporting and external review of clinical trials, IM for dermatology is elaborated using contents of SPIRIT (www.spirit-statement.org) guidelines. Practices followed in IAD are often used as examples. Establishing mutual orientation in MSMT and arriving at a consensus for IM diagnosis and treatment have already been described[2], and thus are not discussed here.

Components of IM patient care protocol

Clinical setting

The required setting is simply an outpatient department, though an inpatient facility would be ideal. Mutually oriented health practitioners from different systems of medicine – Ayurveda, Homoeopathy (optional), Yoga therapists, Ayurveda massage therapists, counsellors and nurses – should work in a team led by a biomedical dermatologist. A compression therapist is essential as part of any team managing lymphoedema patients. The minimal essential requirements include a basic clinical laboratory managed by a laboratory technician and an integrative pharmacy with stocks of essential biomedical drugs for dermatology and basic life support. A decent stock of Ayurveda herbals should also be maintained, as many herbals are seasonal and not available for purchase year-round. A trained nurse should always available during clinic hours to provide basic life support, if required. Regular training sessions are mandatory, covering topics like waste disposal, infection control and basic life support.

Additional facilities essential for patient management at an IM centre are:

(a) *Panchakarma* theatre[7,8]: Area of 800 sq. ft, where patients are prepared for and then receive Ayurvedic procedure-based therapies with an attached wash area.

(b) Drug-manufacturing facility: Herbal medicines may be prepared on site, under the supervision of an Ayurvedic physician, when they are not available for sale. Pulverizing unit for producing personalized prescriptions of Ayurvedic physicians and a drying area for herbs to be used are essential.

(c) Image (photography) acquisition studio: Photography is essential for dermatological education and monitoring patient progress[9]. Digital images provide a useful, realistic and objective record. There should be uniformity in the acquisition of images at baseline and follow-ups for reliable comparison. To achieve this, in IAD multiple factors have been controlled during image acquisition. A 2 sq. m wall covered with black cotton was erected in a 3 m long room as the studio. Images were acquired in JPEG format using a Nikon D-90 Digital Single Lens Reflex camera with 12.3 mega-pixel resolution. The light sources were compact fluorescent lamp domes (27 W × 4). Each patient's whole body surface area was divided into 20 anatomical frames. The images were stored on the protected server using patient ID number. Sub-folders were created for each follow-up. Photographs acquired during each follow-up can be compared to objectively measure treatment outcomes.

(d) IM database, stored on a central server.

(e) Minor operation theatre: Requiring an autoclave, fumigation facilities and a manual fire-based incinerator, a portable biogas unit for disposal of food waste, which can all be maintained by a nurse. Basic life support medicines should be stored here, according to the American BSL protocol[10], and those required for critical care in dermatology[11]. A biomedical waste disposal system is mandatory and in IAD this is linked to Indian Medical Association Goes Eco-Friendly (IMAGE)[12]. When an on-site critical care facility is not available, the IM centre must have arrangements to shift patients to any such facility nearby.

Patient population

Most patients entering into IM management are found to suffer with their disease for many years. Their treatment history tends to have proceeded in the following way: first biomedicine; if it fails to produce the desired results, then use CAM systems such as Ayurveda, Homoeopathy and Unani. These patients often use just one CAM discipline at this point, not a combination of CAM with biomedicine or another CAM system. When such patients present for IM treatment, the disease has been long-established and therefore is more likely to be late stage, for example, a case of grade-3 lymphoedema with warty changes, nodules and multiple bacterial entry points (BEPs) over the thickened skin, resulting in frequent inflammatory episodes. Similarly, psoriasis patients often present with long-term, generalized plaque psoriasis, vitiligo and lichen planus patients often present with disease duration of two or more years[13], whereas other patients present with chronic wounds due to venous or mixed vascular disease. A precise description of each patient is documented in both biomedical and Ayurvedic terms. Patient examination by the MSMT is essential to define a study's patient population. This is in contrast to biomedical clinical trials, where the patient population is defined before a study begins.

Study design

Study design depends on the specific research question[14]. Adaptive designs (adapting a study as it progresses by use of accumulating data) are often useful in IM studies. IM protocols at IAD tend to evolve from case series studies.

Patient recruitment strategy

The process of recruitment should be recorded for every patient. Patients might have been referred by doctors, or may have come for treatment earlier, or exposed to media coverage.

One example of a recruitment strategy to conduct a community-level, non-randomized IM study for lymphatic filariasis (LF) is elaborated as follows[15]. A rapid survey of two endemic LF districts was first performed, in collaboration with District-level Health Officers, Government Malaria–Filaria Officers, Public Health Managers, Accredited Social Health Activists (ASHA) and community-based organizations. Fifty one-day community awareness and medical treatment camps were organized in LF endemic villages near the patient clusters for treatment recruitment[15]. An inaugural public function was held at each camp with local social and political leaders, including patient education classes, skin care and Yoga demonstrations. Patients were educated on LF, its aetiology, environmental factors which may complicate the disease, and disease-associated pathological changes. Using audiovisual aids, BEPs were explained and all attendees were educated on managing them and the importance of doing so[16]. Previous patient outcomes were shown through documentaries. After this immersive experience, many patients were recruited into later IM treatment and trials and had good prior knowledge, before they even had counselling, about what the process would involve.

Treatment counselling

Before any management begins, patients should undergo a detailed counselling session by a dedicated counsellor in their native language, which is carefully documented. Patients and their relatives receive complete details of the treatment programme preferably using disease-specific slide presentations and videos. The session covers potential concordance issues and manages expectations of the patient, explaining the long-term therapy, safety measures, documentation and review systems, possible risks and benefits, costs to be incurred, the various interactions with different members of the MSMT team and the informed consent process. Usually it will take a minimum of 30 min to impart all of the required information. Only those patients who subsequently sign the informed consent documents may receive treatment.

Case records

A robust, patient-specific, case-based system of documentation is required, following a protocol for information-gathering and patient assessment and management. The IAD-case records follow Macleod's biomedical structure[17]. History-taking and systems-based clinical examination come first. Homoeopathic assessment is especially detailed[2] and is included in history-taking. The approach to diagnosis differs in Ayurveda and biomedicine. Systematic examination is not well-developed in Ayurveda and does not exist in Homoeopathy; so the detailed listing of physical signs characteristic of biomedicine is lacking. Separate sections within case records allow entry of clinical signs which do not fit neatly into the biomedical approach. The protocol is 'upgraded' to the next 'version' when MSMT's experience highlights improvements that can be made.

Biomedical examples of examination findings influencing subsequent treatment include the hundreds of skin signs and terminologies identified through dermatological examination. Also, locomotor changes such as postural abnormalities or the claw hand or dropped foot of leprosy, should be identified by 'general medical' examination. Ayurvedic clinical features to determine the personalized treatment, local pathology (*Vikruthi Pareeksha*), determination of digestion pattern (*Agni*), prognostic indicators (such as *Sadhya-Asadhya lakshana* of vitiligo)[18], require understanding of special language usages, which is additionally contextual and can be cultural. This should be taken into account when interpreting traditional texts. The disease condition *Amavatha* refers to the localized action of intermediary products of metabolism and toxic substances (*Ama*) on the joints, resulting in impaired mobility and arthralgia. As in this example, Ayurvedic diagnostic terminology is based on causative factors. Thus, the case sheet must allow for these additional assessments, which do not fall into a biomedical structure. The IAD case-record contains a section for entry of such MSMT discussions.

Outcome measures for each patient were recorded in separate sections, including the Lymphatic Filariasis Specific Quality of Life Questionnaire[19] or Dermatology Life Quality Index (DLQI)[20] for vitiligo. Only objective and reliable outcome measures[21] should be included such as limb circumference and volume measurements, body weight[22] and vitiligo disease activity (VIDA) scoring sheet[23]. Scores for concordance to treatment are also helpful. The IAD case-record includes pre-designed proformas, which record the clinical features known to affect outcomes. An organized, safe and accessible store for case files is essential.

Patient examination

Members of the MSMT of each system of medicine should separately take detailed histories and examine

patients (biomedicine[17], Ayurveda[24] and Homoeopathy[25]), arriving at independent conclusions (provisional diagnosis in biomedicine and *Nidana panchaka*, i.e. five methods of clinical diagnosis in Ayurveda). This is all documented in the same clinical record for each patient, allowing comparison between clinical findings and treatment approach, and identifying commonalities.

Drug selection in Ayurveda

Local disease pathology is among 16 important clinical features to be precisely elicited before selecting an Ayurvedic drug (Table 1). These features are due to different body tissue responses to the pathophysiological processes. Rational Ayurvedic treatment should be formulated on the basis of *Dosha* (three energy principles) derangements. *Sthaneeya* (local) *vikruthi* (pathology) is the most important clinical features in Ayurveda practice. When comparable biomedical terminologies are identified, after examination of the patients together with a biomedical dermatologist, a *Sthaneeya vikruthi* table can be developed, crucial for interdisciplinary understanding. Assessment of any contraindications for Ayurvedic herbal formulations precedes prescription. Identifying contraindications relies upon analysis of *Prakruthi* (constitution), *Sthaneeya vikruthi*, *Nidana panchaka*[26], behavioural patterns, strength and body measurements (Table 1). These assessments add to the personalized nature of Ayurvedic management by taking into account all types of body constitutions and their different responses to therapy[27]. Discussed below are four of the essential clinical features for consideration before Ayurvedic drug selection, which are not directly related to dermatology. The other 12 clinical features used for this have been described previously[27].

Agni describes food digestion and assimilation (sometimes termed *Jatharagni*; *Jathara* = duodenum)[28] and depends on three energy principles involved in physiological balance. These are motion (*Vatha*, comparable to wind in action and properties); metabolism (*Pitta*, comparable to combustion with heat production), and structure (*Kapha*, meaning 'oily' and stable). Digestion also depends on the quality and quantity of food, properties of the soil where vegetables are grown, methods of preparation, combinations of food, usual frequency of food intake and the nature of a person's staple food[29].

If three energy principles are balanced, with regular food intake and thirst, the person will have normal bowel habit, feeling of 'lightness' and the time taken for digesting food is approximately 3 h. This state is termed *Sama agni* (*Sama*: equal) and indicates food is being properly digested[30]. Digestion is disturbed by the predominance of one energy principle, rather than a balance. Digestion when dominated by *Vatha* is erratic (*Vishama*) and the patient struggles to have an eating 'routine'. When dominated by *Pitta* it is excessive (*Theekshna*), due to the increased gastric secretion, and the patient becomes hungry in less than 3 hours after food. When *Kapha* dominates, digestion is reduced (*Manda*), believed to be due to increased gastric mucous secretions and meaning that a patient will take an increased length of time to become hungry after food.

Derangements in *agni* produce additional clinical features. This is based on the disturbance in nourishment of basic body tissues (*Dhathu*) of the patient. The control of assimilation of the 'essences of digestion' (comparable to nutrients) is termed *Dhathu agni*. Ayurveda describes seven of these essences. Clinical features of *Dhathu agni* pathology are listed in Table 2. Assimilation of the nutrients of food into body components is regulated by *Dhathu agni*.

The first basic body tissue to receive nourishment from the absorption of digested food is the lymphatic matter, followed by blood. Nourishment then cascades to other tissues, as listed in Table 2. Although this process is predominantly sequential, Ayurveda describes that all seven *Dhathu agni* essences are also absorbed through different channels from the intestine, dividing the process further.

The principle behind rejuvenation treatment of malnourished patients (*Rasayana*) and male patients with sexual dysfunction (*Vajeekarana*) is similar, aiming to correct the digestive system and nourish the basic body tissues, including the testes and prostate (semen is termed *Shukra dhathu*). *Vajeekarana* reduces sexual dysfunction either by increasing *Shukra Dhathu agni* or providing extra nourishment of *Shukra Dhathu* due to another unknown action of the drug (termed *Prabhava*). The digestive focus of these treatments is despite the fact that these patients may have no apparent abdominal complaints on initial questioning. The success of the rejuvenation treatment is shown through improvement in memory power, intelligence, body strength, improvement in skin tone and lustre, voice and an overall healthier appearance[31]. Successful *Vajeekarana* treatment additionally provides satisfaction during sexual intercourse, increases body strength of the patients and their progeny[32].

The Ayurvedic term *Ama*[33] describes food which is absorbed into the body without having been properly digested, due to the patient's digestion being overall reduced (*Manda agni*) or excessive (*Theekshna agni*). *Ama* has a broader meaning of intermediary products of metabolism and toxic substances too. Undigested food is believed to be in a 'fermented state' in the stomach where it contains harmful elements that might cause disease if absorbed. After absorption, circulating *Ama* could reside in vitiated spaces (*Khavaigunya*) such as on cell membranes, continuing to produce disease. *Ama* blocks *Dhathu agni* channels, recognized by malnourishment of the body tissues (*Dhathu*; Table 1). This explanation in Ayurveda is similar to the biomedical description of diet-induced antigens causing disease through immune

Table 1. Comparable biomedical explanations for Ayurvedic clinical principles, whose understanding is essential to an integrative medicine approach

Major Ayurvedic clinical principles[26]	Comparable biomedical explanation[2]	Essential clinical features which should be elicited
Dosha	Primary life force	Ayurveda believes that there are three primary life forces: *Vatha*, *Pitta* and *Kapha*. The vitiation (impairment) of one or more of these forces may occur due to aetiological factors such as poor diet, harmful environment or psychological factors. For example, excessive intake of non-vegetarian food is believed to be a causative factor for skin diseases; therefore a largely vegetarian diet forms part of the treatment. Disease pathogenesis is split into six types (*Shat-kriyakala*) depending on different effects on and of the *doshas*: (i) Moderate accumulation of a *dosha* – For example, *Vatha* in the intestines, *Pitta* in the duodenum and *Kapha* in the stomach. This is clinically identified by determining aversions towards the aetiological factors and cravings for their opposite, such as cravings for salt in exhaustion (*Vatha*). (ii) Aggravation of a *dosha* in its site of origin – may present with abdominal pain and distension (*vatha* aggravation), sour taste, thirst and heartburn (*pitta* aggravation) or indigestion and the sensation of chest 'fullness' (*kapha* aggravation). (iii) Circulation of a vitiated *dosha* throughout the body. (iv) Localization of a *dosha* in a vitiated space. (v) Manifestation of signs and symptoms. (vi) Stage of complications – Diseases are believed to exhibit signs and symptoms in their fourth stage and complications in their fifth stage. Identifying the stage of complication is important for differential diagnosis. Two possibilities for each dosha are augmentation (*Vrudhi*) or diminution (*Kshaya*): *Vatha* – Augmented *Vatha* causes emaciation, depression and hyperpigmentation of skin. Also sleep disturbance, reduced strength and sensory disturbance. Abdominal distension secondary to constipation, giddiness, tremor and incoherent speech may also be reported. Patients tend to crave heat. Whereas *Vatha* diminution produces exhaustion and a sensation of body 'heaviness'. The patient may seem to be 'lazy' due to difficulty in doing work, including slowness of thought-processes and speech. They have indigestion and excessive salivation. *Pitta* – Yellow discolouration of a patient's stool, urine, eyes and skin is believed to represent an augmented *Pitta*. Patients complain of excessive thirst, insomnia and widespread burning sensation. Patients with reduction of *pitta* present with cold and 'lustreless' skin and indigestion. *Kapha* – Augmented *Kapha* apparently leads to breathlessness, cough and excessive sleep. The patient's skin is classically pale and cold. Patients also complain of body 'heaviness' and of feeling 'lazy'. Diminished *Kapha* leads to palpitations, giddiness, a sensation of chest and head 'emptiness' and joint laxity. Assessment of these parameters is achieved through thorough history-taking, inspection and examination.
Prakruthi	Biological constitution of a patient's body	An assessment of *Prakruthi* is completed by listing various characteristics of a person, as decided by a chart containing 60 points (20 broad groups) based on clinical, mental, behavioural and diet parameters. *Prakruthi* is determined through the primary life force (*dosha*) dominance – either a single *dosha* dominance (*Vathaja*, *Pittaja* or *Kaphaja*), two *doshas* being dominant (*Vahtapittaja, Vathakaphaja* or *Kaphapittaja*), or all three *doshas* being equal and balanced (*Thri-dosha-ja*). A single *dosha*-dominant Prakruthi is uncommon. *Prakruthi* is used as part of the prognostic assessment. If a patient's vitiated *dosha* and dominant *prakruthi* are the same, then the disease is considered to be difficult to manage. For example, hemiplegia is classically believed to be *vatha*-dominant; therefore, a patient with a *vatha*-dominant *prakruthi* (single or in combination with another *dosha*) has a worse prognosis.

(*Contd*)

Table 1. (*Contd*)

Major Ayurvedic clinical principles[26]	Comparable biomedical explanation[2]	Essential clinical features which should be elicited
Dooshya	Derangement of 'basic body tissues' and body excretions	Ayurveda describes seven 'basic body tissues' and three excreta (urine, faeces and sweat). The primary life forces (*doshas*) have the power to augment or diminish these. Regarding skin diseases, the effects of such derangement of basic body tissues (*Dhathugatha kusta*) have been previously discussed[27]. Assessment of *dooshya* is achieved through thorough history-taking, inspection and examination.
Desha	The 'habitat' where a patient resides	Three habitats are recognized in Ayurveda – desert (*Janghala*), fertile (*Anoopa*) and moderate (*Sadharana*), which has *Vatha*, *Kapha* and *Pitta* dosha dominance respectively. The persons living there are more likely to have the diseases due to respective dosha dominance. A patient's food habits will also depend on habitat; for example, spicy and dry foods are more common in dry regions. People living on fertile land are generally better nourished. The subject of *desha* would surely benefit from collaboration with biomedicine. However, it lacks information regarding epidemiology, which is also crucial when examining the effects of where a patient lives.
Vayas	Life stage of a patient	Three life stages are described in Ayurveda: childhood (*Balya*), the middle stage (*Madhyama*) and old age (*Jeerna*). They affect medicine choice, ingredients and dose. For example, purgation treatment is contra-indicated in children, to whom only mild laxatives are given.
Pramana	Body 'measurement'	An assessment of *pramana* is made through inspection and is used to assess an individual's disability.
Sara	Factors indicating firmness or dominance	Ayurveda describes eight factors (*saras*) whose presence or absence should be considered for each patient to determine their overall 'dominance'. Presence of all eight factors indicates excellent strength. Such a patient is better able to tolerate Ayurvedic medication and *Panchakarma* procedures, suffering less from adverse effects. The presence of less than three factors indicates severe weakness. The eight *saras* for consideration are as follows: Skin 'dominance' (*twak sara*) is recognized by oily, soft and healthy skin with delicate, healthy hairs. Blood 'dominance' (*rakta sara*) is identified by the presence of oily and pink ears, eyes, mouth and tongue in a person who is said to be 'charming'. Muscle dominance (*mamsa sara*) is shown by compact yet strong temporal and orbital regions. Excessively oily skin, particularly eyelids, indicates fat 'dominance' (*meda sara*). Broad knee, ankle and mandible joints, large bones and teeth, and broad nails indicate bone 'dominance' (*asthi sara*). 'Long' joints, body 'softness' and oily skin suggest bone marrow 'dominance' (*majja sara*). A strong physique with a broad gluteal region represents semen 'dominance' (*shukra sara*).
Samhanana	Acquired body 'build' or physique	A 'good' *samhanana* would be indicated by proportionate, compact and intact joints with reasonable muscular bulk. This indicates that the patient will tolerate strong medications.
Kala	Seasonal nature and duration of disease	Some diseases manifest during specific seasons or climates. Duration is important for elucidation, as in biomedicine.
Vyayama shakti	Exercise tolerance	The patient's exercise tolerance is identified through history taking and is loosely categorized into three groups: Excellent: Patient exercises daily and experiences no exhaustion following strenuous work. Moderate: Patient irregularly exercises and becomes exhausted after small amounts of work. Minimal: Patient never or very infrequently exercises and is unable to tolerate any strenuous work.

(*Contd*)

Table 1. (*Contd*)

Major Ayurvedic clinical principles[26]	Comparable biomedical explanation[2]	Essential clinical features which should be elicited
Agni	Digestive power	Agni refers to *Jatharagni* (*Jathara* = duodenum) and *Dhathu agni* (*dhathu* is basic body tissue). *Jatharagni* describes food digestion and assimilation. It is affected by the quantity of food intake and time taken for the patient to digest their meals. The control of assimilation of the 'essences of digestion' (comparable to nutrients) and then in to body components is termed *Dhathu agni*.
Satwa	Patterns of behaviour	Different patients will show remarkably different capacities for tolerating diseases. Some tolerate chronic, severe disease states with little complaint, while others may experience symptoms which appear to be disproportionate to the disease severity. It is important to identify this through detailed history-taking; otherwise, it may adversely influence diagnosis.
Sathmyam	An assessment of a patient's dietary habits, aspects may be described as 'compatible' or 'incompatible'	A patient's dietary habits should be recorded in order that their *sathmyam* may be assessed. In India, a patient eating a 'balanced diet' will consume appropriate quantities of ghee, milk and oil, with regular meat and a wide variety of foods. This patient is subsequently accustomed to many tastes (*sarva* = all *rasa* = taste). A less healthy *sathmyam* would be a situation where the patient is accustomed only to a few tastes or to a single taste (*eka* = single *rasa*) due to a more limited diet. Excessive consumption of fried items is also bad. The patient's *sathmyam* should be corrected through education of improved diet patterns.
Bala	Immunity of a patient to infections	Three types of immunity are described in Ayurveda: congenital (*Sahaja*), seasonal (*Kalaja*) and acquired (*Yuktikrutha*). Congenital immunity is identified through examining a patient's *sathmyam, sara* and *satwa*. A patient who possesses good strength and exhibits positive behavioural patterns, who enjoys a balanced diet, tends to have good congenital immunity. A poor congenital immunity would be a contraindication for high potency drugs. Seasonal immunity varies throughout the year, as its name suggests. In summer, individuals exhibit less seasonal immunity than during winter and rainy season. Acquired immunity is improved through balanced diet, moderate exercise and daily activity. Ayurvedic rejuvenation treatments also help.
Roga avastha	Disease stage	Different stages of the same disease are treated with different medicines in Ayurveda. History taking identifies aetiology, prodromal symptoms and pathogenesis of disease and helps to determine the Roga avastha. Although in Ayurvedic 'trial and error' method of drug administration is the most important treatment method.
Bhaishajya	Clinical pharmacology	The different combinations of multimodal interventions, medicine ingredients and 'characteristics', dosage patterns, route of administration, fluid vehicle to take after medicine (*Anupana*) and with medicine (*Sahapana*) should be considered during personalized drug selection in relation to clinical presentation.

complexes. *Ama* may be identified in a patient by a set of vague symptoms. Accumulation of *Ama* results in fainting, excessive salivation, indigestion, tastelessness, laziness, loss of strength, the sensation of body 'heaviness', constipation and symptoms of bowel obstruction[34].

Ama is treated with carminatives (*Pachana*). If it is due to slow digestion (*Manda agni*), appetisers (*Deepana*) are added to the regimen. *Ama* caused by a pathological body tissue (*Dosha*) is known as *Sama*[35]. *Vatha* associated with *Ama* presents with abdominal pain and distension, indicating intestinal pathology (*Pakwashaya*, *pakwa* = digested food, *ashaya* = channel). *Ama* due to *Pitta* derangement presents with oral foul smell, bitter taste and excessive salivation, indicative of duodenum involvement. The sensation of an oral 'coating' is due to *Kapha*, which originates from the stomach. Both stomach and intestine therefore may be sites of disease production.

It is important to determine *Sama* and pathological *Agni* in IM management of dermatology patients, because they cause improper nutrition of basic body tissues. Especially in chronic skin diseases, *Ama* occurring during the course of treatment could increase disease activity and may make medications less effective if they rely

Table 2. Clinical features of basic body tissue pathology (*Dhathu agni*) and malnourishment as described in Ayurveda

The different 'basic body tissues' listed in Ayurveda (*Dhathu*)	Functions of basic body tissue according to Ayurveda*	Ayurvedic description of basic body tissue pathology	Clinical manifestations of diminution of the basic body tissue according to Ayurveda[27]
Lymph/lymphatic system (*Rasa*)	Nourishment of all body tissues	*Rasa Dhathu agni*	Widespread skin dryness, exhaustion, poor work tolerance, phonophobia and fainting episodes.
Blood and vascular system (*Raktha*)	Life support, affects skin colour	*Raktha Dhathu agni*	Patients crave sour and cold foods; skin dryness and unfilled veins seen on inspection.
Muscle tissue (*Mamsa*)	Body structuring and movement	*Mamsa Dhathu agni*	Emaciation, particularly of the neck and gluteal region. Patient commonly suffers with blackouts, joint pains and crepitus.
Adipose tissue (*Meda*)	Oiliness of organs	*Meda Dhathu agni*	Emaciation, with numbness over the lumbar region. Splenomegaly may be palpable.
Bone (*Asthi*)	Body shape, permits upright stance	*Asthi Dhathu agni*	Pain over bony prominences, nail damage or resorption, premature loss of teeth and hair without another identifiable cause.
Bone marrow (*Majja*)	Fills and strengthens bones	*Majja Dhathu agni*	Giddiness and fainting; bones which are easily fractured and produce bony pain.
Semen (*Shukra*)	Reproduction	*Shukra Dhathu agni*	Premature ejaculation, hemato-spermia, severe penile and scrotal pain, comparable to 'burning from hot fumes'.

*When the dysfunction of one basic body tissue is identified, one must also check the other basic body tissues. This is because Ayurveda describes how a major function of each tissue is to 'nourish' the next.

upon the vitiated *dosha* for their therapeutic effect. In this situation, the indicated medicines have to be temporarily withdrawn and carminative medicines prescribed for two weeks to allow resolution. Regular medicine should be restarted after the clinical features of *Ama* subside and normal *agni* features are manifest. This personalized medicine prescription could be likened to reducing confounding factors or adaptive research design in a purely biomedical study.

Integrally linked to *Agni* is *Kosta*, meaning bowel movements[35]. Ayurveda describes 'normal' bowel movements (*madhya kosta*) as opening bowels once daily with semi-solid faeces which passes easily. Constipation (*krura*) is due to erratic *agni* (*vatha* vitiation). If the patients needs to open their bowels after drinking a small quantity of milk (*mrudu kosta*), this represents excessive *agni* (*pitta* vitiation). Kosta must be corrected prior to prescribing Ayurvedic medicines and affect the medicines which may be prescribed. For example, high potency drugs, which take a long time to digest, are not given to *Mrudu kosta* patients. Constipation is a common complaint of chronic skin disease patients and should be managed by daily laxatives (*anulomana*). Bowel movements are related to *Agni* and can reflect digestive system abnormality, which must be studied further by the physician.

The drug selection process is described in a separate branch of Ayurveda known as *Bhaishajya kalpana*, comparable to the clinical pharmacology of biomedicine. Each drug is explained in terms of its characteristics: (1) Taste (*rasa*) – six tastes described. (2) Chemical and physical properties (*guna*) – 20 options exist. (3) Potency (*veerya*) – separated into 'hot' (*Ushna*) and 'cold' (*Sheetha*). These terms refer not to the temperature, but to the metabolic effects of a food. There is no known consistent correlate of this concept in Western medicine[36]. (4) Post-digestive savour (*Vipaka*) – three savours described. (5) Unexplained action of the drug (*Prabhava*). All drugs possess the first four properties, but a few drugs exhibit a fifth property, producing actions which cannot be explained in the Ayurvedic literature.

These five characteristics of a drug determine its compatibility in deranged *Agni*, *Dhathu Agni* and *Ama* conditions.

'Hot potency' is identified when a person feels dizziness, thirst, fatigue, sweating and a burning sensation after consuming a drug[37]. They may also experience increased appetite due to action of the drug on the digestive system. The intake of 'cold potency' drugs gives the sensation of being refreshed, reducing sweating and increasing 'lustre' of the skin[37]. Although there are no explanations for the action of topical Ayurvedic agents on the skin, early unpublished work at IAD shows that inflammatory, *Pitta*-dominant skin diseases such as psoriasis respond well to 'cold potency' drugs such as *Chandanadi thailam*. *Kapha* and *vatha*-dominant skin

diseases, such as hypertrophied lichen planus respond well to hot potency drugs such as *Maha marichadi thailam*. Ayurvedic medicines are mostly used in compound forms and multi-component mixtures, occasionally including minerals. When drugs of equal potencies are combined, smaller quantities are required.

Post-digestive savour is a secondary 'taste' due to the processing of food through digestion[38], identified by its action on the body. Drugs with a sweet (*madhura*) post-digestive savour are purported to reduce pain, xerosis, erythema and burning; however, they may produce the sensation of body heaviness. Sour (*amla*) savour drugs increase appetite, but may produce heartburn. A pungent (*katu*) post-digestive taste reduces the sensation of body heaviness and improves the taste of foods.

Dosage patterns of drugs, including time of intake and the fluid vehicle to be taken with or after medicine are other factors to be considered during medicine selection. A patient less than 16 years of age is prescribed half dosage of Ayurvedic medicine.

In Ayurveda, skin diseases are all generally believed to be associated with 'excessive nourishment'. Medications prescribed for skin diseases should produce increased thirst and appetite, normal bowel movements and the sensation of lightness of the whole body (*Langhana*)[36].

Medicines are generally selected based mainly on potency[39] because, unlike taste and post-digestive savour, drug potency is not affected by *Agni*. For example, *Glycyrrhiza glabra* L. has a sweet taste, cold potency and a sweet post-digestive savour. *Tinospora cordifolia* has a pungent and astringent taste, hot potency and but a sweet post-digestive savour; therefore the taste here changes during the digestive process, but potency remains unchanged. *Chandanadi thailam* has cold potency and is prescribed for the inflammatory lesions of psoriasis. It reduces the inflammation and burning sensation associated with pitta dominance. Maha marichadi *thailam* used for lichen planus has a hot potency. It reduces the elevated, hypertrophied and xerotic lesions associated with *Kapha vatha* vitiation. Semecarpus anacardium is indicated in skin disorders due to its hot potency. Though drug has rejuvenation action which should be avoided in skin disorders, its hot potency is responsible for the beneficial action.

Prabhava (the unexplainable action) of a drug can be the most important factor for its clinical use, such as the unexplained action of skin repigmentation of *Psoralea corylifolia* for vitiligo. *P. corylifolia* is beneficial for skin diseases in general due to its hot potency. However, in general, hot-potency drugs are not recommended in vitiligo as most of them fail to produce repigmentation. This is where an integrated approach becomes useful because, ancient though Ayurvedic texts fail to explain the repigmentation action of psoralia, the photosensitization action of psoralen (active ingredient of *P. corylifolia*) is well-described in dermatology.

Diet and drug in Ayurveda

As in biomedicine, Ayurveda includes dietary recommendations. These also depend on body mass index (BMI) and overall nutrition, *agni*, *kosta*, staple food, quantity of food, type of job and also clinical pharmacology (*Bhaishajya*). The restricted dietary items in skin disorders are 17 varieties of 'incompatible' food (*Virudha ahara*) and food items which are slow to digest (*Guru*) or sour (*Amla*). Excessive non-vegetarian or milk products should be avoided as they are believed to provide excessive nourishment and thus aggravation of skin disorders[2].

Careful determination of disease stages for right drug selection

Different stages of disease (*Roga avasta*) also require different medicinal treatment in Ayurveda. Stages are often described in a different manner compared to biomedicine and if a clinician fails to identify the stage correctly, treatment may not work.

An example to illustrate the effect of disease stage on Ayurvedic treatment is seen with lichen planus (LP). Different types of LP include lichen ruber planus, generalized and acute lichen planus, chronic lichen planus and bullous lichen planus. Lichen ruber planus describes erythematous, flat-topped polygonal papules which retain the skin creases and vary in size from pinpoint to more than a centimetre diameter. This is comparable to a sign called *Pidaka*, a *Pitta*-dominant Ayurvedic skin presentation. Hypertrophic LP is chronic, violaceous to black coloured, thickened skin with roughened edges. Lesions are severely itchy, which may interfere with sleep and severely affecting quality of life. This is comparable to the description of *Kapha*-dominant skin lesions (Figure 1).

The development of hypertrophic lesions greatly lengthens the course of the disease, as they may persist for many years. When LP lesions are eventually treated, an area of pigmentation and scarring may remain and there is often some degree of atrophy. This is comparable to Ayurvedic *Vatha*-dominated disease. Therefore this shows how different stages of the disease have different *Dosha* dominance, requiring different drug selection. Lichen ruber planus is treated with *Eladi thailam*, a sesame oil preparation; hypertrophic lesions are treated best with *Guggulumarichadi thailam* or *Maha marichadi thailam* to reduce *Kapha*. The post-inflammatory pigmentation with atrophy is managed through medicated ghee, indicated for *Vatha* dominance.

Differential diagnosis is known by the comparable Sanskrit term '*Vyavachedaka nidana*'. A literature search using the term 'Vyavachedaka nidana' yielded no results on PubMed[40], AYUSH portal[41] or DHARA[42]. The structured discussion on differential diagnosis as in

biomedicine does not exist in Ayurveda. These clinicians depend on history-taking and 'trial and error' drug administration with observation of clinical changes on follow-up. Primary symptoms, site of origin, primary life forces, and basic body tissues (*Dosha* and *Dhathu*) affected and associated symptoms are the factors considered to differentiate between diseases. Errors may arise as these factors tend towards being subjective with no objective measures considered. One illustrative example is psoriasis, where there are four different comparable Ayurvedic terminologies. *Kitibha* and *Eka* describe skin resembling chronic plaque psoriasis, *Mandala* is similar to guttate psoriasis, while *Vipadika* resembles palmoplantar psoriasis (Figure 2). Each of these has different *Dosha* dominance and therefore different treatments.

Another demonstrative example is rheumatic diseases. The clinical picture of polyarthralgia initially with *Ama* symptoms (elaborated above) and in the later stages of the disease associated with skin manifestations is described as *Amavatha* (comparable to the arthralgia) associated with auto-immune connective tissue diseases[43] and medicines prepared with *Ricinus communis* are used. Small joint inflammation, subsequently extending to larger joints is termed *Vatharakta* (comparable to rheumatoid arthritis or Henoch Schoneline perpura), treated with herbal formulations containing *Tinospora cordifolia* (*Amrutha*). Arthritis which affects weight-bearing joints, associated with crepitus, is termed *Sandhigatha vatha* (comparable to osteoarthritis) and is managed with *Alpinia galanga* (*Rasna*). In a 'trial and error' pharmacological treatment method (*Upashaya*), drugs of either opposite or equal potencies to the cause of the disease or the disease itself are used to identify the exact *Dosha* dominance and best manage joint pains[24]. Interestingly the application of oil (either mixed herbal or sesame oil), increases pain in acute *Amavatha* (*Ama* aggravation) and reduces pain in *Sandhigatha vatha* (*Vatha* amelioration).

Intervention adherence

Drugs of biomedicine and CAM are administered simultaneously. IM relies upon a fusion of Western models of patient care and Eastern traditional management models[44], resulting in a complex, multimodal treatment plan.

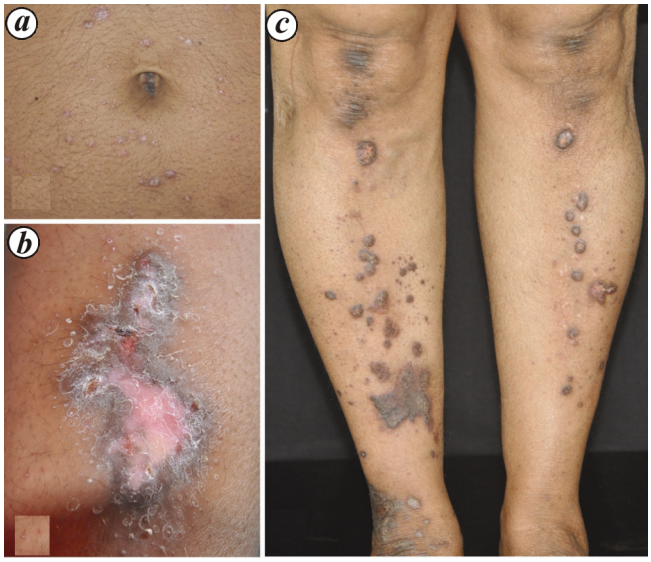

Figure 1. Different stages of lichen planus (*Roga avasta*) with different nomenclature and dosha dominances in Ayurveda. ***a***, Lichen rubour planus lesions, compared to erythematous (*raga*), annular (*mandala*), papules (*pidaka*) of *dadru* as explained in *Charaka Samhitha*, one among 18 skin diseases. This stage of the disease is *kapha pitta*-dominant. ***b***, Hypertrophic lichen planus: hypopigmentation observed at the middle, surrounded by violaceous colour. The lesions are thickened (*ghana*), elevated (*utsedha*), with rough edges (*ruksham Bahi*). There are excoriations caused by intense itching. There is a single lesion; *kapha vata* dominance without whole body involvement. ***c***, Hypertrophic lichen planus lesions in lower limbs with violaceous (*shyava*/*asitha*), elevated (*utsedha*), xerosis on inspection (*ruksha*), xerosis on palpation (*parusha*), uneven surface (*khara*); there is and there was a history of pruritus (*kandu*). The lesions are *kapha vatha*-dominant with no specific nomenclature in Ayurveda.

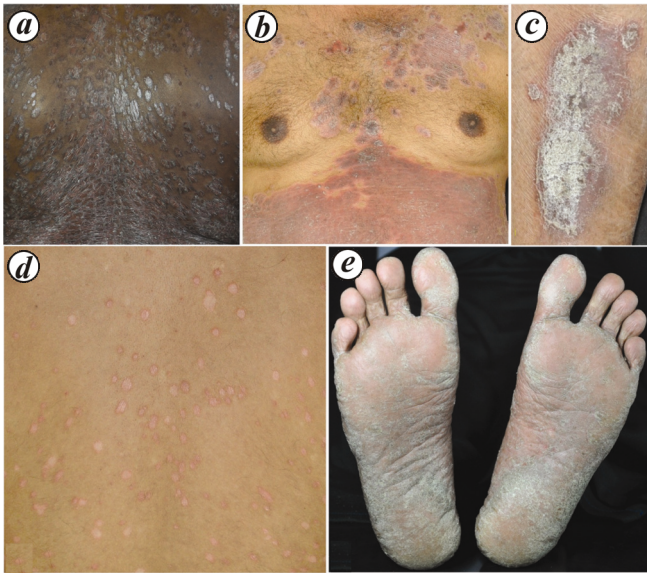

Figure 2. The differences in comparable descriptions of Ayurveda for psoriasis. Chronic plaque psoriasis is comparable (***a***) *Eka kusta*, (***b***) *sidhma* and (***c***) *rshyajihwa* in Ayurveda. *Eka kusta* has absence of sweat (*aswedana*), generalized (*Mahavasthu*) and scales like fish flakes (*mathsya shakalopama*). The lesions are *kapha* and *vatha*-dominant. *Sidhma* has xerosis on inspection (*ruksha)*, dusty scales (rajo ghristam), white (*Alabu pushpa varnam*). Lesion in is thick (*ghana)*, annular (*mandala*), both are not descriptions of *sidhma*. The lesions show excoriations due to pruritis. The *rshyajihwa* lesions are reddish edges (Rakthantha), blackish in middle (*Antha shyavam*), xerosis on palpation (*Parusha*), thin (*Thanu*), slimy (*Kleda*), uneven surface and with boils (*Karkasha Pidikoschitham*). Elevated (*Samunnatha*) with *vatha pitta* dominance. (***d***) Guttate psoriasis is comparable with *mandala kusta*, with annular (*Mandala*), erythematous (*Raktha varna*), xerosis on inspection (*Ruksha*), xerosis on palpation (*Parusha*), uneven surface (*Khara*) of lesions. (***e***) Palmoplantar psoriasis has painful (*theevra vedana*) fissures of soles and palms (*pani pada sphutana*), comparable to *Vipadika* with *vatha* dominance.

Although the drugs of biomedicine and CAM may be given simultaneously, there are important differences between treatments which must be fully understood to allow proper adherence. This requires commitment of the healthcare delivery team, to impart the necessary information to the patients. 'Intervention adherence' in IM is defined as 'the ability and extent to which patients follow the therapy instructions of their healthcare team, especially in the community'. Monitoring adherence is particularly important for an IM approach to patient management, where an accurate measurement of each patient's medication history is essential for elucidating which aspects of treatment are effective and for the 'trial-and-error' Ayurvedic approach to be prescribed.

Here we consider adherence to IM lymphoedema management; a previous community-based trial estimated[15] this at 72.4%. The following strategies to both ensure and monitor adherence are used, some of which are particularly useful for patients who are unable to attend regular follow-up.

(1) Routine follow-up: At every appointment, a counsellor checks the patient's understanding of all steps of treatment which should be followed at home and whether these are all being done, assisted by a check-list and adherence questionnaire. The doctors and therapists also assist with this and repetition helps drive home the message of adherence that is crucial for successful outcomes.

(2) Pharmacy records: Patients mostly purchase their medicine from the IAD's own integrative pharmacy. Every individual's supply is monitored, showing how well they are progressing.

(3) Telephone counselling: Counsellors may speak to patients over the phone to check concordance and reinforce the message of its importance. This may be a formalized call between follow-ups or a random check; it can also be done via Skype, if possible.

(4) 'Home Care Manual': This document is given to every patient and encourages them to call IAD with any adherence issues.

(5) Reminder letters and/or e-mails: Sent to those patients who have fallen out of contact or who may have changed their telephone number. These include adherence questionnaires and reminders.

Patient education

This aspect of management often carries little emphasis in industry-sponsored trials, but can strongly influence treatment outcomes. Patients must be educated sufficiently through classes and written materials so that they can continue treatment at home. They should be actively questioned about their treatment to ensure full understanding. This also emphasizes adherence, as described above. Second, most of the patients are chronic sufferers, with multiple comorbidities, many of whom have begun to feel hopeless about finding a cure for their illness. Counselling therefore has the additional and important role of instilling hope in such patients and their families.

Concomitant care

In these complex patients, it is important to consider all associated diseases and co-morbidities. These should be explored and documented in the case sheet, along with details of various doctors responsible for their management. Concomitant medications should usually be continued but should be listed in the IM drug chart, so that any herbal drugs known to cause interactions can be avoided[45]. Literature search can help prevent drug interactions and close monitoring should be done to identify any unexpected interactions which may arise. Regular monitoring of a patient's primary disease and updates on co-morbidities should be recorded by the team. Additional critical care counselling should be given to high-risk cardiovascular and cerebrovascular patients and their family members.

There are certain specific situations where concomitant medications should be discontinued, if possible. For example, micronized, purified flavonoid fraction and diuretics for lymphoedema patients[46]. This is because, in general, diuretics such as frusemide do not improve lymphoedema. However, it is important to consider the individual before discontinuing the diuretic. Yoga, which is important for IM management of lymphoedema, can precipitate heart failure by raising venous pressure during massive fluid shifts. In these cases diuretics may actually be required. Herbomineral CAM preparations should be checked for approval by the country's regulatory authority and discontinued unless approved.

Rescue medication

'Acute on chronic' conditions are common in patients with multiple co-morbidities. A common example is cellulitis, affecting patients with chronic lymphoedema. When this occurs, IM should be stopped and acute care medicines be administered by biomedical physicians. Similarly, acute exacerbations of lichen planus require prednisolone, whereas erythrodermic exacerbations of psoriasis require methotrexate. These 'rescue medicines' should be withdrawn once the patients recover from acute exacerbation; IM is generally restarted one month later. In Ayurveda, 'rescue medication' is used when the patient's *agni* becomes deranged during the course of treatment.

Treatment outcomes

IM 'primary' outcome measures should evaluate clinical improvement and consider adverse effects. These should be measured using objectively validated methods. 'Secondary' outcomes include subjective or minor outcomes.

Ayurvedic *Phalashruthi*[47] are traditional outcome measures for administered medicine. They are listed in traditional textbooks, although not for all formulations. In an IM centre, comparable biomedical terminology for each *phalashruthi* should be identified in the literature[2,48,49], or identified by the MSMT[2]. Ayurvedic doctors prefer to use *phalashruthi* as their primary outcome measure, helping them to direct their traditional treatments. Since objective outcome measures are generally not found in the traditional literature, Ayurvedic doctors rely on *phalashruthi* and other clinical guidelines in Sanskrit texts to determine patient outcomes. As greater number of patients are managed, Ayurvedic doctors can gradually adapt patient care protocols and introduce biomedical objective outcomes.

At the start of IM disease management, the MSMT should agree on a set of primary and secondary outcome measures, including deciding how exactly these will be measured and integrating the outcome measures of the various medicine disciplines. Precisely how this is achieved is discussed elsewhere[2]. When available, systematic reviews from the Cochrane library are used to select evidence-based outcome tools and measures. The core outcome measures in effectiveness trials (COMET) Initiative (http://www.comet-initiative.org/) helps standardize outcome measures for specific disease conditions. In the case of lymphoedema, Partsch *et al.*[21] have discussed the consensus outcome measures.

Managing adverse events

WHO's definition of an adverse drug reaction (ADR) is 'a response to a medicine which is noxious and unintended, and which occurs in doses normally used in man'[50,51]. This can be expanded to include traditional medicines, for example, events occurring with topical Ayurvedic oils in their normal recommended doses mentioned in the traditional literature. When adverse effects of treatment are suspected, the Naranjo scale[52] may help confirm or refute this. If confirmed, the 'common terminology criteria for adverse events v4.0' (CTCAE) is useful to identify descriptive terminology to record the effect[53]. In dermatology, ADRs are commonly cutaneous and the pattern produced should be extensively searched in the literature[54], to guide subsequent management and exclude any life-threatening events.

Other considerations for an ADR are its severity and whether it has been previously described with the prescribed medication(s), or is totally unexpected. The very nature of IM is that each component interacts with multiple others and, because it is a relatively novel management strategy, the new drug combinations open the possibility of new ADRs[55]. Therefore, safety measures should be performed in all patients after the initial three months of treatment[50]. Urine analysis and measurements of renal and hepatic function, full blood count and erythrocyte sedimentation rate should be completed. Repeated ECGs should also be taken with echocardiography if required, to detect cardiac-related ADR. Despite the apparent 'opportunity' for them to emerge, so far only a few ADRs to Ayurvedic topical and oral medications have been identified.

Timeline for follow-up visits

The MSMT must jointly decide about a patient's follow-up. This is decided by considering the stage and any complications of the primary disease, the patient's stress level as assessed by his/her 'mental symptoms' as highlighted by use of the comprehensive Homoeopathy questionnaire, distance of patient's home from the outpatient setting, ability to carry out complex IM at home, social support available and any comorbidities. Patients who live far away and are therefore not easily able to attend follow-up should be encouraged to keep in regular contact through e-mail, telephone or Skype.

Evidence of effectiveness

Data collection

Patient information should be recorded in a structured manner. This can be consistently achieved using a checklist format for recording history-taking and examination. The IAD utilizes specific case-records for different diseases, using existing biomedical and Ayurvedic literature to help formulate them[56] and improving each through use. Through the process of developing these specific case-records, the MSMT is further educated about the diseases and about data entry. Internationally accepted scoring systems may be included when appropriate or novel IM scoring systems are created[19,48]. Modified versions of existing systems or unpublished measurement scales should not be used unless they can be validated, as this may introduce bias in data collection.

It is important to introduce a system of checks for the standardization of data-recording, thus enhancing the quality of data collected and reducing bias. This should include identifying and addressing any missing or incomplete data, inaccuracies or excessive variability in measurements. Random page numbers, generated using Microsoft Excel, can be used to direct these checks by random sampling of large case-records. During the daily clinical rounds, the MSMT members may also review past data entry and the records should be assessed for completeness before filing away when a patient is discharged.

Data management

For use in a study, data need to be entered into a customized electronic database from the paper case-sheets. Raw

and non-numerical data should be coded to facilitate storage, review, tabulation and analysis. The coding explanation should also be clearly accessible in the database.

Data monitoring

This describes the process of regularly reviewing the data being collected via the case-sheets and how they are being recorded. This ensures that the study questions being asked are being answered with the data collected. To most effectively carry out this improvement process, it is best to seek the advice and unbiased opinion of other experts in the field, as well as the patients themselves[57]. However, this may take several years to reach perfection.

An example of this has been the IAD's monitoring of data for their IM management of LF. This has been achieved through seven, three-day national colloquiums since 2005, attended by those involved in protocol development and international, unbiased LF experts. LF patients receiving IM management also attend and daily clinical rounds are conducted during the colloquium, where patients are examined by the attending experts. Patients also have the opportunity to express any questions or concerns regarding their disease or treatment and these are addressed. As a result of these colloquiums and data monitoring, the patient care protocols can be improved and thus data collection as well.

Auditing

This is another essential part of the internal improvement and quality assurance process and should be done by at least two members of the MSMT. It involves examining case-records, discharge summaries and then checking that the information transfer to the electronic database is being done accurately and completely.

Ethical clearance and review of study

A local ethics committee (Institutional Review Board; IRB) should review study proposals and monitor IM study ethics as they progress. An IRB is currently not required by Indian law before study registration, but is an important way to ensure ethical research. As described above, extensive counselling and explanation take place before IM treatment begins, to ensure fully informed consent. This includes consent for image acquisition, any procedures and use of non-identifiable patient data and/or samples for research. Recent discussion has centred on structured methods to develop trial consent forms[58].

Confidentiality

Patient identity must be masked before data interpretation and publication. This is easily achieved by replacing patient-identifying information by patient ID. The database matching ID to identifiable information is then kept separately and access restricted to the treatment team and those involved in data audit and analysis. Occasionally journals request raw data before publication; so it is best to preempt this when taking consent.

Conflict of interest

Non-financial, academic and association-related conflicts of interest are widespread in India, especially creating hostility among professionals of biomedicine and CAM and with the potential to introduce bias into research[59]. Groups must therefore try to remove this as much as possible, especially for an IM approach which requires collaboration of modern and traditional medicines[2,60]. Academic volunteers must also share the mantra of the research organization – always putting the patient's best interests before their academic agenda[61].

Publication policy

Although major clinical studies are undertaken in the Indian Government's CAM institutions, albeit with methodological errors[62], a large number of studies are not published. At this early stage of development of CAM and IM literature, institutions conducting IM studies should aim to publish all their data, even if the results are negative[63] and ideally follow the relevant BMJ guidelines[64].

Collaborations

Fifteen years of IM development have shown that some disease stages previously believed to be 'untreatable' do respond to this approach of collaboration between medicine principles. Indeed, IM teams 'can achieve more together, and more quickly, by combining different expertise from different niche areas than working alone'[65]. Establishment of relevant collaborations is essential for joint, comprehensive and sustainable IM research activities by incorporating the academic knowledge, technological competency, methodology and design from other disciplines of science. These disciplines may include biomedicine, pathology, physiology, bioengineering, Ayurveda, Yoga, Homoeopathy and other traditional Indian systems of medicine. These research collaborations, especially with molecular biology, pathology, biochemistry, biotechnology departments and traditional drug manufacturers who can assist with reverse pharmacology studies[66], will significantly advance IM research. A noteworthy example of contribution to the IM approach came from the International Lymphoedema Framework (http://www.lympho.org/), a London-based

charitable platform dedicated to the lymphoedema community.

Discussion

Since IAD's first publication on IM[67], the IM protocol development has become more comprehensive and transparent involving all stakeholders, especially patients and international subject-matter experts. Our clinical methods for IM, especially drug selection in Ayurveda, initially focused on lymphoedema and certain dermatological diseases actively developed over the past 15 years. Principles of IM therapeutics for other diseases, especially the practicalities of simultaneous biomedicine and herbal medicine administration, are still under development. Successful IM programmes appear to be built upon biomedical standards of diagnosis, outcome measurement and patient safety. For the credibility of clinical research, including in IM, it must be possible for external groups to replicate studies; therefore the IAD IM protocol is presented in the SPIRIT statement guidelines[68]. This will also help the structuring of future publications in IM, in particular by highlighting the MSMT structure.

Advancing IM clinical methods requires the collaboration of multiple disciplines and team members with diverse backgrounds. IM clinical methods of dermatological examination, including from an Ayurvedic perspective, are available for use by other group[27]. These were first validated and elaborated for lymphoedema and vitiligo[2] and now are being adopted for studies of lichen planus and other diseases, which are difficult to treat[48,69].

Working increasingly closely with Ayurveda physicians highlighted the need for explanation of further Ayurvedic principles not detailed in our previous work[27]. Therefore, Ayurveda clinical methods pertaining to digestion, which are closely linked to drug selection and necessary for understanding the IM approach, are emphasized here. All clinical manifestations of *dosha* vitiation in Ayurveda are included in tables and texts. All those included in the list should be considered in each patient, though they may appear as vague, general complaints to a biomedical doctor. Some of these manifestations may become aggravated during the course of disease management due to an initial error in Ayurvedic diagnosis. This is additionally likely if there are clinical time constraints, because the clinical methods of Ayurveda are comparatively long-winded. Indeed, the very nature of Ayurvedic treatment involves a trial-and-error approach to management. Integration of studies of biomedicine will bring more objectivity to IM patient care protocols. At this stage of development of IM, only proven laboratory techniques should be used. Adapting the latest molecular diagnostics that occasionally needs an additional interpretation on false positive or negative results, requiring complex standardization methods for laboratory methods would add to the ambiguity of IM protocols.

Diet is an important consideration in Ayurveda, whose pharmacological treatments may cause diet–drug–body interactions not formerly known in biomedicine. Patients who do not follow Ayurvedic diet recommendations may suffer from disease aggravation, despite the correct drug selection. This is believed to be due to derangement of the patient's digestive power (*agni*) and thus the availability of the 'essences' of digestion (*dhathu agni*). In such situations, drugs under trial should be withdrawn temporarily and the digestive system 'normalized' using other drugs not directly related to the primary disease. Such treatment options form an essential part of unique, personalized medicinal approach of the Ayurveda, comparable to 'rescue medicine' for acute exacerbations of chronic diseases, as described in biomedicine. Describing the apparently unconnected clinical constellations, the unfamiliar technical terms and CAM approaches for inclusion in IM protocols are a challenge. Therefore, we recommend the use of SPIRIT guidelines.

Accessible descriptive details of Ayurvedic patient selection criteria and outcome measures are essential for a biomedical doctor to understand the complete IM process, especially because of the total absence of technology-based studies in Ayurveda. Indeed, the experience of the Ayurvedic clinicians is of utmost importance to treatment success because of the complex mixture of history and observations during the clinical methods. The Indian Council for Medical Research has made participation of both biomedical and Ayurvedic physicians mandatory for IM studies. However, participation of two systems of medicine does not guarantee successful IM treatment; IM participants should be 'intense clinicians and intense researchers at the same time'. Nobel laureate Joseph L. Goldstein has described such studies as 'patient-oriented research' (POR) and such a physicianas 'PORer'[70]. POR is performed by physicians who observe, analyse and manage individual patients. Developing IM protocols and clinical methods occurs through POR. The father of modern POR, Archibald Garrod (1857–1936), linked the black urine of a patient to alcaptonuria and advanced the concept of the inborn error of metabolism[71]. Many recent examples exist, notably Nobel laureate Barry Marshall, who identified *Helicobacter pylori* as a cause of gastric ulcers, amongst others[72,73]. POR requires an 'intimate knowledge of disease' and the ability to recognize patterns across multiple patients.

The major limiting factor for developing successful IM leads over the last decade, has been the lack of research and development funding. In India, IM case-series and non-randomized controlled trials, even if published[6], rarely lead to any funding for higher evidence-level studies. This seems to mostly be due to the mindset of committee members and reviewers in India, who limit funding to groups whose initial work has been developed through

randomized controlled trials (RCTs)[74]. RCTs are too expensive for IM practice and indeed are frequently not warranted for early work. IM studies should be designed to answer specific research questions and new treatments have to gradually climb the levels of evidence[14]. Observational studies as part of an IM protocol development process also contribute development of clinical methods.

The current approach towards the use of CAM therapies based on ancient guidelines is likely to experience a paradigm shift through emerging collaborations between IM/CAM physicians and molecular and tissue-level research. This process will help these therapies to realize their clinical potential[75] and modified usage options through incorporation with biomedicine. This requires research collaboration with pathologists, molecular biologists, basic scientists, pharmaceutical manufacturers and related disciplines. IM is already trailblazing this process, which will hopefully help solve the worrying impending paralysis of clinical IM academia.

It is crucial to structure IM manuscripts carefully to make the complex approach of IM accessible to a greater readership and to increase the likelihood of publication in biomedical journals. Editors and reviewers are accustomed to an introduction – methods – results–and–discussion structure. Fitting an IM and CAM study around an existing biomedical journal structure is not always possible or optimal. The IAD has instead adopted the SPIRIT principles and we recommend the SPIRIT framework to bring uniformity for IM and CAM studies. In this article, we have communicated the protocol which has been developed, utilizing the SPIRIT guidelines together with our wealth of practical knowledge from 15 years of experience, as to how a prospective IM study may be conducted. The SPIRIT guidance alone incorporated several international guidelines[76]. We have proposed a way of planning, carrying out and subsequently describing an IM study, rather than focusing on the initial study design stage. Adherence of IM studies to such a protocol, which follows the SPIRIT recommendations, would improve their approach, accuracy, ethics, structure and subsequent write-up, benefitting journal editors, reviewers and all stakeholders, especially the patients.

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