Meeting Report

# GRAPPA — Group for Research and Assessment of Psoriasis and Psoriatic Arthritis Stockholm, May/June 2006

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GRAPPA (Group for Research and Assessment of Psoriasis and Psoriatic Arthritis) grew from an international collaborative study to determine new classification criteria for psoriatic arthritis (CASPAR)[1]. During the CASPAR project a few of the collaborators met to discuss expanding the purpose of the collaboration, modeling the organization on the Assessment in Ankylosing Spondylitis Working Group (ASAS). Subsequently, the first meeting of this group was held in New York in August 2003.

From the outset GRAPPA was designed to be inclusive and tried to pull together many different groups, including researchers and thought-leaders in psoriatic arthritis (PsA) and psoriasis. The idea was to form a consortium of rheumatologists, dermatologists, radiologists, geneticists, methodologists, epidemiologists, and representatives from patient service leagues who would contribute to the field of PsA and PsO. Subsequent meetings, usually held adjacent to major international rheumatology and dermatology meetings, have focused on identifying and initiating research projects, advancing standardized criteria for psoriasis and PsA registries, and developing treatment guidelines. Much of this work has been possible as a result of educational grants from the pharmaceutical industry, although GRAPPA itself is an independent organization working within the Northwest Arthritis and Osteoporosis Institute (NAOI), a nonprofit organization based in Seattle, Washington. Today, as many as 200 people participate in GRAPPA including representatives of the biopharmaceutical industry. European and US participants make up the majority of the group but there are representatives worldwide, creating a truly international effort. This report summarizes the achievements of this group over the first 3 years and reviews the highlights of the meeting that took place in Stockholm, May/June 2006. The meeting was organized adjacent to the first joint dermatology/rheumatology meeting under the auspices of the International Federation of Psoriasis Associations.

## The aims and structure of GRAPPA

Despite the ad hoc nature of the organization, day to day operation was facilitated by Philip Mease of Seattle and Dafna Gladman of Toronto. Philip Mease was also able to engage excellent administrative support through a Seattle organization called Health Advocacy Strategies (http://www.hastrategies.com/). Initially, the steering committee membership was by invitation and people became members of the group without restriction. Discussions began at an early stage to impose some form of administrative structure in order to formalize the decision-making and to make the group as democratic as possible. A review of existing and similar organizations was undertaken and a steering committee finalized the proposed structure. This draft constitution was then circulated to the whole membership, modified, and finally approved by a majority of members. As the constitution required an elected committee structure, the initial electoral process was conducted by E-mail in early 2006 and the results, with the adoption of the constitution and election of officers, were announced at the meeting in Stockholm. The initial committee structure and aims of the GRAPPA group are given in Tables 1 and 2. The terms of office require the officers to serve a maximum of 3 years in office, thus ensuring an appropriate sharing of work, and many other members of the organization are actively involved through participation in subcommittees (see below). New members are now required to submit a brief curriculum vitae and need a proposer and seconder from the existing membership (http://grappanetwork.org). There are no dues.

GRAPPA has developed relatively quickly over the last 3 years, transforming from an ad hoc meeting to a constitutionally governed democratic group. Further, during these 3 years the group has had several notable achievements, listed in Table 3. The future agenda and organizational structure mean that the group will not now stand still — the future plans are discussed later.

## The Stockholm meeting

The First World Psoriasis and Psoriatic Arthritis Conference held in Stockholm May 31 to June 4, 2006, was unique in that it was the first meeting devoted to psoriasis and PsA attended by dermatologists, rheumatologists, and representatives of patient organizations. The GRAPPA meeting, which preceded

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*Table 1*. The elected committee structure of GRAPPA.

| Committees |
|---|
| Executive Committee |
| Executive Committee Committee Members: |
| Dafna Gladman (R), President |
| Philip Mease (R), Vice President |
| Philip Helliwell (R), Treasurer |
| Wolf-Henning Boehncke (D), Secretary |
| Gerald Krueger (D), Member at large |
| Christopher Ritchlin (R), Member at large |
| Steering Committee |
| Steering Committee Committee Members: |
| Wolf-Henning Boehncke (D) |
| Jürgen Braun (R) |
| David Fiorentino (D) |
| Oliver FitzGerald (R) |
| Dafna Gladman (R) |
| Alice Gottlieb (D) |
| Philip Helliwell (R) |
| Arthur Kavanaugh (R) |
| Gerald Krueger (D) |
| Philip Mease (R) |
| Peter Nash (R) |
| Kim Papp (D) |
| Abrar Qureshi (D) |
| Christopher Ritchlin (R) |
| Vibeke Strand (R) |
| William Taylor (R) |

D: dermatologist, R: rheumatologist

*Table 2*. The aims of GRAPPA.

- Provide a forum for networking and communication between international researchers in rheumatology and dermatology, industry, patient service leagues, and regulatory agencies
- Provide the opportunity for in-person meetings and intranet communication to share knowledge and research findings, and to develop or conduct collaborative research, education, and other projects
- Develop and validate a criteria set for the definition of PsA
- Review, develop, and validate effective and feasible outcome measures for the assessment of PsA and psoriasis
- Promote the development of national and international collaborative registries of patients with PsA and psoriasis to standardize the data obtained and learn more about the natural history of the disease as well as its genetic foundation
- Work closely with representatives of patient service leagues to promote public education and awareness of PsA and psoriasis
- Work closely with representatives of biopharmaceutical companies to promote and conduct research on effective therapies
- Work closely with representatives of regulatory agencies to establish appropriate guidelines for regulatory approval of new therapies
- Work with other professional bodies, such as the American College of Rheumatology and American Academy of Dermatology in the US, equivalent bodies in other countries, and OMERACT, to promote knowledge of research about PsA and psoriasis within the context of those disciplines
- Develop treatment guidelines for PsA and psoriasis

*Table 3*. The achievements of GRAPPA 2003-2006.

- Publication of a state of the art review of PsA and psoriasis as a supplement to the Annals of Rheumatic Diseases (available at no charge online: http://ard.bmjjournals.com/).
- Development of evidence-based review of PsA treatments (J Rheumatology 2006;33:1417-56. www.jrheum.com).
- Development of core set of PsA and psoriasis domains of inquiry to be used in clinical trials research through consensus process, finalized at OMERACT in 2004 (J Rheumatology 2005;32:2246-76) and 2006. Domains of enquiry include composite joint assessment, skin, enthesis, dactylitis, spine, patient global, function/quality of life, and immunohistology.
- Intranet for GRAPPA members launched in 2004; this provides a way to communicate and post documents for group review and input (http://grappanetwork.org).
- Meetings held adjacent to American Academy of Dermatology (AAD), EULAR, OMERACT, ACR, and European Academy of Dermatology and Venereology (EADV) (2004, 2005, 2006).
- First face to face interdisciplinary meeting held in New York (2003). Second major meeting of dermatologists and rheumatologists Stockholm 2006.
- Vibrant committee structure (see Table 5).

the main meeting, thus benefited by having both dermatologists and rheumatologists attending in roughly equal numbers. This was in contrast to earlier meetings adjacent to specialist societies, which were attended by the predominant specialty, either rheumatologists or dermatologists, depending on which society meeting was taking place. A summary of the meeting program is given in Table 4.

## Review of treatment guidelines

*A. Kavanaugh and C. Ritchlin*

Arthur Kavanaugh (Professor of Medicine, University of San Diego, San Diego, CA) reviewed the development of treatment guidelines. The initial part of this process had been an evidence-based review of existing therapies for psoriasis and PsA, recently published in *The Journal of Rheumatology*[2]. Prof. Kavanaugh discussed the methodology and obstacles to the next step in the process, the development of international guidelines (defined as "Systematically developed statements to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances"). PsA is a het-

*Table 4*. Program of the GRAPPA meeting in Stockholm May/June 2006.

- Introductory remarks (P. Mease)
- Review of treatment guidelines process (A. Kavanaugh, C. Ritchlin)
- Review of OMERACT (D. Gladman)

**Hot Topics**

  - CASPAR classification criteria and its incorporation with clinical trials and clinical practice (P. Helliwell)
  - Development of tools to identify instruments to evaluate PsA by dermatologists (S. Feldman)
  - Quality measures (A. Kavanaugh, W.H. Boehncke)
  - Methotrexate/prednisone use in PsA (A. Gottlieb)
  - Patient perspective on domains and outcome measures (P. Mease)

- Governance/business part of the meeting (P. Helliwell)

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erogeneous disease and thus it was difficult to synthesize guidelines to cover all aspects of it in an abbreviated manner. The lack of validated disease activity tools and precise prognostic data was highlighted, together with the need for more precise data on subgroups in order to optimize stratification. As a starting point it was suggested that the focus was on the patient with polyarticular peripheral arthritis, the commonest subgroup. With this in mind, GRAPPA has been developing and validating outcome measures in the domains of signs/symptoms, structural integrity, functional status, participation, and quality of life (see OMERACT update in the next section). As a corollary to this it was noted that guideline exigency has been driven by the introduction of novel immunomodulatory therapies. A further problem with any international guideline is the need to encompass sensitivity to local factors (mostly economic) and cultural differences.

Prof. Kavanaugh indicated that most of the treatments we now use for PsA are not evidence-based, or are based on poor quality evidence. A number of articles have commented on assessing the quality of evidence systematically and, where possible, these should be used to evaluate therapies[3,4]. The relatively new drugs, including the biologics, have a much better and more comprehensive evidence base, thus devaluing recommendations covering the whole spectrum of treatments. Expert opinion is not a good basis for recommendations, but in the absence of good quality evidence, this is what we may have to resort to in PsA.

**Review of the OMERACT workshop**

Dafna Gladman, the newly elected first President of GRAPPA, presented a review of the OMERACT process, the workshop on PsA held in Asilomar, California, in 2004 (OMERACT 7[5]) and the module held in Malta in 2006 (OMERACT 8). The workshop in Asilomar had identified the domains that were important for developing outcome measures for clinical trials in PsA. The top 5 domains were (percentage voting for): joint activity (99%), patient global (96%), pain assessment (94%), physical function (91%), and skin disease (86%). The objectives of the module at OMERACT 8 were: (1) Achieve consensus on the *core set* of domains to be assessed in PsA clinical trials and in longitudinal observational cohort studies; (2) Review and endorse *outcome measures* used to assess these domains based on evidence derived from clinical trials; and (3) Set up a new *research agenda* to identify other assessment tools.

After a number of presentations, participants had an opportunity to vote once again on the core domains and, after discussion in breakout sessions, a further opportunity to vote. As a result the GRAPPA steering committee was able to construct a set of essential core domains, and to include 2 other categories — "necessary but not mandatory" and a "research agenda" category. The domains were presented in a diagram format (Figure 1) following a suggestion by Vibeke Strand (Division of Immunology, Stanford University, Palo Alto, CA, USA). Although a number of validated instruments are available for the core domains, the most appropriate instruments for measuring the other domains still need to be decided, and further work by GRAPPA is currently under way[6].

**The essential core set of domains**

- Peripheral joint activity
- Skin activity
- Patient global
- Pain
- Physical function
- Health related quality of life

**Domains that are "necessary but not mandatory"**

- Enthesitis
- Dactylitis
- Radiology
- Fatigue
- Physician global
- Acute phase reactants
- Spinal
- Nails

**Domains on the research agenda**

- Tissue analysis
- Magnetic resonance imaging
- Ultrasound
- Computer tomography
- Participation

*Figure 1*. The outcome domains voted for at OMERACT 8.

**CASPAR criteria**

The meeting next considered some new and relevant data and controversial subjects needing attention by the GRAPPA group.

Philip Helliwell reported on the CASPAR study — an international collaboration to examine the performance characteristics of existing classification criteria for PsA and to develop new criteria based on a large cohort of cases and controls. The CASPAR study had started collecting data in 2002 and the main results have now been published[1]. The new criteria, given in Table 5, contained items relevant to the skin and joints included dactylitis and one radiological criterion. It was pointed out that the Moll and Wright criteria used by many investigators[7] were encompassed within these new criteria (ensuring sensitivity), but that the additional features

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*Table 5*. The CASPAR criteria.

| Inflammatory Articular Disease (joint, spine, or entheseal) | |
|---|---|
| With 3 or more points from the following: | |
| 1. Evidence of psoriasis (one of a, b, c) | |
| (a) Current psoriasis* | Psoriatic skin or scalp disease present today as judged by a rheumatologist or dermatologist |
| (b) Personal history of psoriasis | A history of psoriasis that may be obtained from patient, family doctor, dermatologist, rheumatologist, or other qualified healthcare provider |
| (c) Family history of psoriasis | A history of psoriasis in a first- or second-degree relative according to patient report |
| 2. Psoriatic nail dystrophy | Typical psoriatic nail dystrophy including onycholysis, pitting, and hyperkeratosis observed on current physical examination |
| 3. A negative test for rheumatoid factor | By any method except latex but preferably by ELISA or nephelometry, according to the local laboratory reference range |
| 4. Dactylitis (one of a, b) | |
| (a) Current | Swelling of an entire digit |
| (b) History | A history of dactylitis recorded by a rheumatologist |
| 5. Radiological evidence of juxtaarticular new bone formation | Ill-defined ossification near joint margins (but excluding osteophyte formation) on plain radiographs of hand or foot |

Specificity 98.7%, sensitivity 91.4%. * Current psoriasis scores 2, whereas all other items score 1.

enhanced the specificity compared to Moll and Wright. However, due to the long disease duration of cases included in the study the criteria are not yet applicable to early disease, although anecdotal reports at the meeting suggested that they worked equally well in early disease.

Other points of note about the criteria were discussed. Further elaboration of the entry criterion — Inflammatory articular disease (joint, spine, or entheseal) — is required: what exactly do rheumatologists mean by inflammatory articular disease and how can this be conveyed in criteria? The absence of spinal features in the CASPAR criteria was also noted. In fact, about 13% of the controls in this study had ankylosing spondylitis, so the statistical analyses were influenced *against* selecting spinal features as characteristic of PsA. Although it has been suggested that the spondylitis of PsA is qualitatively and quantitatively different from that seen in classical ankylosing spondylitis[8,9], these differences did not appear as discriminating features. Had the controls consisted only of cases of rheumatoid arthritis then it is possible that the spinal features would have appeared in the final criteria set. Enthesitis was also omitted from the final criteria set because, despite the hypothesized pivotal pathologic expression of this feature[10], a good number of the control population had both clinical and radiological enthesopathy[11].

For now the CASPAR criteria should be used for clinical trials so that cross-study uniformity can occur and permit us to move toward homogeneity in immunohistologic studies. Further development of the criteria is under way, with clinical and radiological examination of a population of subjects with psoriasis and articular symptoms (by screening questionnaire), a prospective study of a population of subjects with early disease, and a closer look at the subgroup of patients with anti-cyclic citrullinated peptide antibodies[12].

**Development of tools to identify instruments to evaluate psoriatic arthritis by dermatologists**

Steve Feldman (Professor of Dermatology, Pathology and Public Health Sciences, Wake Forest University School of Medicine, Winston-Salem, NC, USA) led this discussion. Several members of GRAPPA had recently participated in an exercise led by Dr. Feldman to identify important clinical features that would help a dermatologist identify relevant articular disease in association with psoriasis, which initial treatments to carry out, and when to refer. Although this exercise had produced a wide spectrum of opinions, some consensus was found. The majority of respondents thought that dermatologists should ask their patients about joint pain and stiffness and that they should perform at least some form of joint examination. The examples suggested varied from examining only the symptomatic joints for signs of inflammation to a full screening examination of the kind suggested for general physicians[13].

Most rheumatology respondents thought that the dermatologist should not perform any laboratory or radiologic investigations, but opinion was divided, as it was for the exact timing of referral. Specific features of PsA such as dactylitis and enthesitis were thought to be indicators for referral to a rheumatologist, and ocular features such as uveitis as a reason for referral to an ophthalmologist. Most rheumatologists thought that it was acceptable for dermatologists to prescribe

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nonsteroidal antiinflammatory drugs (NSAID), but to refer if any further treatments were thought necessary. In conclusion, Prof. Feldman noted that rheumatologists seem confident in dermatologists' ability to diagnose PsA and dermatologists can treat with NSAID, but beyond that rheumatologists want to be involved. He expressed that this was not that different from how he would want rheumatologists to approach the skin involvement in this disorder.

This subject stimulated much discussion, and highlighted the different responsibilities and expertise of the specialties involved in treating this disease. Work is currently under way by GRAPPA to look at screening tools for PsA in patients with psoriasis, and a reliability exercise is planned for 2007 where rheumatologists and dermatologists can examine complementary clinical skills. Rheumatologists seemed confident in diagnosing psoriasis, but a dermatologist pointed out that there are as yet no validated clinical criteria for psoriasis, hampering the development of an appropriate screening tool.

**Update on clinical quality**

Wolf-Henning Boehncke (University of Frankfurt, Frankfurt, Germany) presented a summary on quality measures being introduced for dermatologists in Germany. Such measures are loosely aligned to appraisal and outcome in the UK, and are also under consideration in other countries such as the USA. It is likely, in appropriate healthcare systems, that reimbursement will be dependent on demonstrating these quality measures. These are likely to include both process and outcome measures (yet to be defined), as well as treatment choice decisions. This is where GRAPPA may have a role, and it is likely that these measures will be aligned to those under development for use in clinical trials in addition to links to the international guidelines.

Prof. Kavanaugh outlined developments in the USA. A complex structure of quality checks, called pay for performance (P4P), is gaining acceptance by those who pay for healthcare. Although not universal at the moment, it is anticipated that all payers will subscribe to such a system eventually. The proportional split of quality measures in California is currently clinical domain 50%, patient experience domain 30%, investment in information technology 20%, and a bonus opportunity, 10%. An example of a nonrheumatological clinical domain would be low density lipoprotein screening and control.

A number of problems currently exist with this system, including multiple variations. It is expected that the indicators will be evidence-based and ultimately that higher quality will become the norm. If the system works, poorly-performing doctors will be reimbursed less. A similar system introduced for primary care in the UK has seen some primary care physicians make significant salary increases, although the targets can become an obsession. Hopefully these "quality indicators" will not be achieved at the expense of good patient care rated by other, less tangible means[14].

Further information can be obtained from the resources given in Table 6.

**Toxicity of methotrexate in psoriatic arthritis and psoriasis**

Rheumatologists have been using methotrexate (MTX) for over 20 years in rheumatoid arthritis (RA) and dermatologists even longer in the treatment of psoriasis. As MTX is a known hepatotoxic drug most dermatologists and rheumatologists warn against even moderate alcohol intake and follow a cautious monitoring program. Initially this program advised periodic liver biopsies according to the cumulative dose received. More recently, the trend in RA has been to discontinue routine liver biopsy and to monitor using liver biochemistry[15]. However, dermatologists using MTX for psoriasis continue to advise caution and recommend liver biopsies according to the cumulative dose. These observations, together with a comprehensive review of the literature, were presented by Prof. Alice Gottlieb (Professor of Dermatology, Tufts University, Boston, MA, USA). A recent metaanalysis found that patients with psoriasis taking MTX were more likely than patients with RA to have advanced histological changes on liver biopsy (7.7% vs 2.7%, respectively; $p = 0.003$) and histologic progression (33.1% vs 24.3%; $p = 0.02$)[16]. For some reason patients with psoriasis and PsA are more susceptible to the hepatotoxic effects of MTX. Whether this is due to other factors, such as alcohol intake, not appropriately controlled for in the studies, or a greater degree of obesity with concomitant hepatic steatosis in psoriasis patients, remains unclear. However, new data suggest that hepatotoxicity with the new biologic drugs is also greater in patients with psoriasis and PsA compared to RA[17], again highlighting that these are not similar diseases and should have unique toxicity monitoring schedules. The problem is particularly relevant to rheumatology, where MTX and

*Table 6*. Relevant organizations involved in quality measure development in the US.

- Centers for Medicare and Medicaid Services (CMS): www.cms.hhs.gov/quality/pfqi.asp. Physician Focused Quality Initiative (PFQI); Physician Voluntary Reporting System (PVRS); Doctor's Office Quality (DOQ) project.
- American Medical Association (AMA): www.ama-assn.org/ama/pub/category/2946.html. Physician Consortium for Performance Improvement (PCPI). Major source of material for NQF, AQA.
- Ambulatory Quality Alliance (AQA): www.ambulatoryqualityalliance.org. Started in 2004 by America's Health Insurance Plans, AAFP, ACP, and Agency for Healthcare Research and Quality (AHRQ). Leader in selecting performance measures for physician practices (26 as of May 2006).
- National Committee for Quality Assurance (NCQA): www.ncqa.org. A supplier of performance measurements, especially for managed care. Invited American College of Rheumatology and others to participate in back pain measures.
- National Quality Forum (NQF): www.qualityforum.org. Nonprofit group developing performance measures.

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*Table 7*. GRAPPA subcommittees and their respective chairs.

| |
|---|
| Governance: Philip Helliwell |
| Immunohistology: Oliver FitzGerald |
| Imaging: Desiree van der Heijde |
| Quality of life/function/participation: Philip Mease |
| OMERACT: Dafna Gladman |
| Patient global assessment: Alberto Cauli |
| Publications: Dafna Gladman |
| Research: Philip Helliwell |
| Treatment guidelines: Arthur Kavanaugh |
| Website: Peter Nash |
| Skin: W.H. Boehncke |
| Peripheral joint assessment: Dafna Gladman |
| Spinal assessment: Ignazio Olivieri |

other disease modifying drugs may be given uninterrupted for long periods of time, whereas dermatologists tend to use bursts of therapy to clear the skin disease. Fortunately for dermatologists, psoriasis usually leaves no damage in the skin, a situation unhappily not true for the joint disease.

### Future directions for GRAPPA

The First World Congress of Psoriasis and Psoriatic Arthritis in Stockholm was the first "stand-alone" joint dermatology/rheumatology meeting of its kind (excepting the first small GRAPPA meeting in New York). Its apparent success has encouraged the International Federation of Psoriasis Associations to hold another such meeting, again in Stockholm in 2009. The GRAPPA meeting held as part of this congress for the first time also brought together a large number of dermatologists and rheumatologists, and was so productive that further meetings are planned for 2007. GRAPPA has established a subcommittee structure (Table 7); each of these committees has a research agenda and is independently pursuing it, reporting back to the GRAPPA steering committee and to the GRAPPA membership as a whole.

What are the benefits of GRAPPA membership? Members are kept apprised of current research and data relating to diagnosis, treatment, and etiopathogenesis of psoriasis and PsA. They are asked to contribute to research in these areas. Members are also available to participate in meetings held separately and adjacent to rheumatology and dermatology meetings. Membership is open to all those interested in psoriasis and PsA, but prospective members are required to submit a short curriculum vitae online and to have a proposer and seconder from within the existing GRAPPA membership.


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