COPE guidelines on good publication practice

The Committee on Publication Ethics (COPE) was founded in 1997 by a group of UK medical editors who wished to discuss specific examples of possible research and publication misconduct that they were currently facing. A few, such as the editors of the *Lancet* and *BMJ*, were full time professional editors with a large publishing staff and ready access to expert advice. Most, however, were more isolated part time editors who had received no formal training in publication issues. Additional committee members provided expertise on medical ethics, law, and the practical consequences of actions such as "whistleblowing". The discussions of cases by COPE, published regularly in anonymised form,[1 2] focus on the practicalities of what **should** and what **could** be done in each specific case. These case discussions have proved useful not only to guide appropriate action in individual situations but also as a learning resource for other editors. Importantly, such illustrative cases have highlighted the need for more generic guidelines for good practice on a wide spectrum of research and publication issues.

In April 1999 COPE organised an open one day meeting in London to discuss draft guidelines on good publication practice. Attendance was good with input not only from European and North American editors but also the UK General Medical Council, the Royal College of Physicians, and the pharmaceutical industry. The various research and publication misdemeanours that may be unearthed by the editorial and peer review process were fully debated. The emphasis, however, was on **what action** should be taken by the editor once possible misconduct was suspected or confirmed. The guidelines were modified in the light of those discussions and are now published[2] and available on the web site:

www.publicationethics.org.uk

Although of potential interest to a wide and diverse audience, these guidelines mainly address **practical issues** and therefore are of particular value to authors, editors, editorial board members, and peer reviewers. The first part of the guidelines considers 10 specific areas—namely:

- Study design and ethical approval
- Data analysis
- Authorship
- Conflicts of interest
- Peer review
- Redundant publication
- Plagiarism
- Duties of editors
- Media relations
- Advertising.

Each is firstly defined and then appropriate standards and conduct for each are specified under "action". For example, the sections on "Study design" read as follows:

Definition

Good research should be well justified, well planned, appropriately designed, and ethically approved. To conduct research to a lower standard may constitute misconduct.

Action

(1) Laboratory and clinical research should be driven by protocol; pilot studies should have a written rationale.
(2) Research protocols should seek to answer specific questions, rather than just collect data.
(3) Protocols must be carefully agreed by all contributors and collaborators, including, if appropriate, the participants.
(4) The final protocol should form part of the research record.
(5) Early agreement on the precise roles of the contributors and collaborators, and on matters of authorship and publication, is advised.
(6) Statistical issues should be considered early in study design, including power calculations, to ensure there are neither too few nor too many participants.
(7) Formal and documented ethical approval from an appropriately constituted research ethics committee is required for all studies involving people, medical records, and anonymised human tissues.
(8) Use of human tissues in research should conform to the highest ethical standards, such as those recommended by the Nuffield Council on Bioethics.[3]
(9) Fully informed consent should always be sought. It may not always be possible, however, and in such circumstances, an appropriately constituted research ethics committee should decide if this is ethically acceptable.
(10) When participants are unable to give fully informed consent, research should follow international guidelines, such as those of the Council for International Organisations of Medical Sciences (CIOMS).[4]
(11) Animal experiments require full compliance with local, national, ethical, and regulatory principles, and local licensing arrangements. International standards vary.
(12) Formal supervision, usually the responsibility of the principal investigator, should be provided for all research projects: this must include quality control, and the frequent review and long term retention (maybe up to 15 years) of all records and primary outputs.

Similarly, this is the section on "Duties of editors":

Definition

Editors are the stewards of the journals. They usually take over their journal from previous editor(s) and always want to hand over the journal in good shape. Most editors provide direction for the journal and build a strong management team. They must consider and balance the interests of many constituents, including readers, authors, staff, owners, editorial board members, advertisers, and the media.

Action

(1) Editors' decisions to accept or reject a paper for publication should be based only on the paper's importance, originality, and clarity, and the study's relevance to the remit of the journal.
(2) Studies that challenge previous work published in the journal should be given an especially sympathetic hearing.
(3) Studies reporting negative results should not be excluded.
(4) All original studies should be peer reviewed before publication, taking into full account possible bias due to related or conflicting interests.
(5) Editors must treat all submitted papers as confidential.
(6) When a published paper is subsequently found to contain major flaws, editors must accept responsibility for correcting the record prominently and promptly.

The second part of the guidelines summarises the principles involved when dealing with suspected misconduct, advises on how to investigate both serious and less serious misconduct, and then suggests eight possible sanctions that may be applied (separately or in combination and ranked in approximate order of severity). Finally, details of other guidelines on research ethics and published codes of conduct are listed in an Appendix.

COPE has no statutory powers and the guidelines are intended to be advisory rather than prescriptive. Although COPE consulted widely in the development of the guidelines, it is expected that they will evolve with time. They will be reviewed and refined as necessary each year.

In common with many editors of other biomedical journals these gguidelines were endorsed by the editor of the *Annals*, who feels that they usefully summarise acceptable, expected standards of conduct by authors, reviewers, and editors. The *Annals* has a tradition of interest in all aspects of professional conduct relating to research and publication, and has recognised the importance of appropriate process and editorial responsibility when misconduct arises.[5] We hope that submitting authors and reviewers for the *Annals* will read the COPE guidelines with interest and join the editor and his board in advancing awareness of the issues involved, and in promoting the highest standards of ethical conduct for research and publication.

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1 *The COPE report 1998.* London: BMJ Publishing Group, 1998.
2 *The COPE report 1999.* London: BMJ Publishing Group, 1999.
3 Nuffield Council on Bioethics. *Human tissue: ethical and legal issues.* London: Nuffield Council on Bioethics, 1995.
4 Council for International Organizations of Medical Sciences (CIOMS). *International guidelines for ethical review of epidemiological studies*. Geneva: WHO, 1991.
5 Doherty M. The misconduct of redundant publication. Ann Rheum Dis 1996;55:783–5.

Anti-TNFα: a new dimension in the pharmacotherapy of the spondyloarthropathies !?

Introduction and overview

The therapeutic options for treatment of the spondyloarthropathies (SpA), especially for ankylosing spondylitis (AS), are limited. Physiotherapy is important and nonsteroidal anti-inflammatory drugs (NSAIDs) provide significant symptomatic benefit, as has been shown in many studies, and recently in a six week/one year trial.[1] Apart from sulfasalazine, a disease modifying antirheumatic drug, which many rheumatologists use to treat patients with peripheral arthritis and gut disease in early and in active stages of SpA, few innovative treatments have arisen in the past decades since indometacin was developed.[2] The Cox-2 selective agent rofecoxib, recently introduced, causes fewer gastric ulcers but is no more effective than established NSAIDs.[3] The efficacy of rofecoxib in ankylosing spondylitis (AS) has not been studied to date. Up to 20% of patients with AS do not respond well or at all to NSAIDs.[4] Corticosteroids are effective when applied locally intra-articularly[5] but not systemically in most patients—an interesting difference from rheumatoid arthritis (RA), the pathophysiological basis of which is unclear. Interestingly, quite a few rheumatologists use methotrexate to treat AS,[6] though there are no randomised trials for this indication.

However, possibly positive effects of thalidomide[7] and of pamidronate[8] for the treatment of AS were recently reported from two open studies. Both drugs work, at least partly, by blocking the proinflammatory cytokine tumour necrosis factor α (TNFα),[9 10] which is also the target of recently introduced new treatments for the treatment of RA[11] and Crohn's disease.[12] Shortly after the initial experience of our group with anti-TNF in AS[13] and of others in psoriatic arthritis,[14] both for the first time reported in Boston at the American College of Rheumatology meeting 1999, several studies with "biological" agents acting against TNFα in SpA were reported. One study from our Belgian colleagues is published in this issue of the *Annals*.[15]

Tumour necrosis factor α blockade

Tumour necrosis factor α is a cytokine that is mainly produced by monocytes and macrophages and, to a lesser degree, by T cells. Two specific receptors, a 55 kDa and a 75 kDa, are present on many cell types. TNFα mediates inflammatory and immunoregulatory activities. Effects on cells, such as lymphocyte activation and fibroblast proliferation, on mediators, such as other cytokines—for example, interleukin 1 (IL1), IL6, and IL8, chemokines, prostaglandins, and metalloproteinases, and on the vasculature by promoting angiogenesis, upregulation of adhesion molecules, and transendothelial migration of leucocytes, have been well described. In vitro and in animal models TNFα causes fever, pain, and cachexy, mobilises calcium from bone, and induces apoptosis (see review[16]). All these mechanisms are proinflammatory but, additionally, TNFα has important physiological functions in immune responses against pathogens and may contribute to suppression of autoimmunity and malignancy.[17] Blocking these functions might lead to undesired side effects.

Biological agents blocking TNFα

The antibody used in both the Belgian and the Berlin study was infliximab, the first antibody which was available to treat patients with RA. Infliximab is a chimeric human murine monoclonal class IgG1 antibody (Infliximab, cA2, Remicade, Fa Essex/Centocor). The efficacy of anti-TNFα in Crohn's disease is remarkable because Crohn-like gut lesions have been detected in a significant percentage of patients with SpA.[18] Other agents also act against TNFα, such as the TNFα 75 kDa receptor IgG1 fusion protein (etanercept (Enbrel), Fa Wyeth/Lederle), which has also been proved to be effective in patients with RA when treatment with methotrexate alone was insufficient.[19] It is unclear whether etanercept works in Crohn's disease. The mode of action of these antibodies is probably not identical. However, this issue is beyond the scope of this article.

Anti-TNFα treatment in patients with active ankylosing spondylitis

In the study reported in this issue[15] spinal pain of 7/11 patients with AS improved significantly at two and six weeks after anti-TNFα was given as an induction treatment at weeks 0, 2, and 6. Several years after the description of TNFα mRNA in sacroiliac biopsy specimens of patients