British Bureaucracy Stymies Use of TNF Inhibitors

BY JONATHAN GARDNER
London Bureau

Nearly half of British rheumatologists report that they are unable to prescribe approved drugs for rheumatoid arthritis patients because of financial caps and other constraints placed by their local National Health Service trusts, according to a recent survey.

Rheumatologists reported barriers to prescribing infliximab and etanercept for rheumatoid arthritis patients meeting the guidelines set forth by the National Institute for Health and Clinical Effectiveness (NICE). NHS trusts in England and Wales are required to provide any drug or treatment meeting NICE's clinical and cost-effectiveness standards (Rheumatology 2006 Oct. 11 [Epub doi:10.1093/rheumatology/kel333]).

The survey's authors, Dr. Lesley Kay and Dr. Ian Griffiths, of the musculoskeletal unit at Freeman Hospital in Newcastle-Upon-Tyne, England, sent questionnaires to all 509 consultant rheumatologists who were members of the British Society for Rheumatology. A total of 136 responses on behalf of 252 consultant rheumatologists were received.

Despite NICE's guidelines, 56 of the returned questionnaires, or 42%, representing 115, or 46% of the rheumatologists covered, reported some type of limit on anti–tumor necrosis factor–α therapies such as infliximab or etanercept, the authors wrote.

'The fact that different funding organizations set different restrictions has led to variation of access for equally affected patients to effective treatment.'

Of those reporting limits, 40 said they were in the form of caps on funding or the number of rheumatoid arthritis patients allowed the treatment, 12 reported limits on staffing to meet patient needs, and 4 reported lack of other facilities. Forty-eight respondents also reported a waiting list for such therapies, according to researchers.

Ninety respondents said they are able to prescribe anti–tumor necrosis factor agents for ankylosing spondylitis or psoriatic arthritis in at least some circumstances, leaving 33% of consultant rheumatologists unable to prescribe the therapies for those patients, the researchers wrote.

"The fact that different funding organizations set different restrictions has led to variation of access for equally affected patients to effective treatment, depending on where they live," the authors said. "Long waiting times for patients to receive these drugs once a decision to prescribe has been made are not uncommon, which will add further to their deterioration and compromise their likely outcome."

The organization representing NHS trusts would not comment directly on the survey, but did defend the decisions of its members. "[Primary care trusts] receive a fixed allocation of money to deliver all the services for their local community and have to take difficult decisions on competing priorities," Nigel Edwards, director of policy at the NHS Confederation, said in a written statement.

"For example, this year many PCTs have been faced with decisions about spending money on expensive drugs and cutting waiting lists.

"The decisions that PCTs take are informed by professional executive committees made up of doctors and nurses, as well as managers," Mr. Edwards said. "These committees decide what the local priorities are, and, as every community is different, it is not surprising that they often reach different decisions.

"Many primary care trusts also have active ways of engaging their communities in the decisions they make, and naturally, communities will have different views and priorities themselves." ■

OCs Lower Rheumatoid Factor, While Smoking May Increase It

BY MIRIAM E. TUCKER
Senior Writer

Oral contraceptive use is associated with reduced rates of rheumatoid factor seropositivity in women without rheumatoid arthritis, while cigarette smoking may increase the risk, reported Shailaja S. Bhatia of the University of Colorado, Denver, Dr. Darcy S. Majka of Northwestern University, Chicago, and their associates.

The oral contraceptive (OC) finding is consistent with previous data suggesting a protective effect on the development of rheumatoid arthritis (RA), while previous data on the impact of smoking have conflicted.

Taken together, the results of this study suggest that OC use, and possibly cigarette smoking, act very early in the development of the immune dysregulation that occurs in RA, the investigators reported (Ann. Rheum. Dis. July 2006:DOI:10.1136/ard.2006.060004).

The study population comprised 304 women who had at least one child with the HLA-DR4 allele, which is associated with both RA and type 1 diabetes. (All were participating in a study on the autoimmunity of type 1 diabetes.) After the elimination of 6 women with self-reported RA, the remaining 298 were questioned about symptoms and signs related to RA and completed a risk factor questionnaire. All underwent 68-joint count examinations and were tested for RF and for HLA-DR4 subtypes.

Of the 298 women, 10.4% (31) tested positive for RF. Women who had ever used OCs were less likely to be RF positive than were those who had never used OCs (odds ratio 0.21).

Conversely, women who smoked 20 or more packs of cigarettes per year were 12.5 times more likely to be RF positive than were those who had never smoked, the investigators reported. After the researchers adjusted for age, education, and smoking, those women who had ever used OCs were still significantly less likely to be RF-positive (adjusted odds ratio 0.20). Similarly, smoking 20 or more packs per year was also independently associated with positive RF, compared with never smoking (adjusted odds ratio 56.4).

Oral contraceptive use and cigarette smoking act very early in the development of the immune dysregulation that occurs in RA, study results suggest.

Risk factors found to not be associated with RF positivity included age, ethnicity, educational level, a history of type 1 diabetes or RA in the woman or a family member, smoking less than 20 pack-years of cigarettes, duration of OC use, number of pregnancies, history and duration of breast-feeding, the use of injectable hormones or hormone therapy, and consumption of regular or decaffeinated coffee, the investigators reported.

The mechanism underlying this effect may be that the synthetic hormones in OCs drive the immune system toward T-helper-2 cytokine responses and decreased production of proinflammatory and other cytokines, leading to T-helper-1–associated RA-specific cellular autoimmunity, the investigators speculated. ■

First Report Made of Cutaneous Eruption With Adalimumab Therapy

MANCHESTER, ENGLAND — For the first time, a patient being treated with adalimumab for rheumatoid arthritis has developed a subepidermal pustular eruption, wrote Dr. Preeti Athavale in a poster session at the annual meeting of the British Association of Dermatologists.

Cutaneous reactions have been reported previously for the anti–tumor necrosis factor (TNF)–α agents, including injection site reactions and systemic reactions that occur during infusions. However, it had been expected that adalimumab would have fewer side effects than its predecessors, according to Dr. Athavale, of the department of dermatology at Chesterfield (England) Royal Hospital.

The 37-year-old patient had had debilitating rheumatoid arthritis for 20 years, but had no history of skin disease. She had previously received treatment with cyclosporine, infliximab, and etanercept without success. About 8 months after she began taking adalimumab, she developed painful, itchy pustules on her arms, thighs, and chest. These flared approximately 2 days after she received her twice-monthly adalimumab injection and never entirely cleared, said Dr. Athavale.

Biopsy of a pustule and adjacent skin on the arm revealed a subepidermal neutrophilic pustulosis. Immunofluorescence studies looking for evidence of immunoglobulins and complement were negative, and overall, the findings were not consistent with a primary dermatosis.

The adalimumab was stopped 3 months later for lack of efficacy, and the pustular eruption settled within 1 month. It has not recurred, Dr. Athavale reported.

There have been a few reports of skin reactions to adalimumab, mainly injection site reactions and nonspecific rashes. There also has been one case report of an erythema multiforme–like reaction that cleared when the drug was withdrawn (Arthritis Rheum. 2004;50:1690-2).

—Nancy Walsh