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Editorial

Depression in rheumatoid arthritis—underscoring the problem

> The greatest mistake in the treatment of diseases is that there are physicians for the body and physicians for the soul, although the two cannot be separated.
>
> Plato (427–347 BC)

The management of chronic disease is a major challenge for global health care in the 21st century. The World Health Organization estimates that by the year 2020, depressive disorders will be second only to ischaemic heart disease in the worldwide burden of disease [1]. Rheumatoid arthritis (RA) is the most common chronic inflammatory joint disease, affecting 0.5–1% of the population. It has long been recognized that the two conditions are associated, with conservative estimates of the prevalence of depressive disorder in patients with RA ranging between 13 and 20% [2–4]. These estimates control for the overlap between the symptomatology of RA and depression. This is a higher prevalence than might be expected from clinical practice. However, recent data from the British Society for Rheumatology Biologics Register [5], looking at baseline comorbidity levels in over 7000 patients starting biological treatment, showed that 19% of these patients had been given a formal diagnosis of depression at one time. These rates are 2–3 times higher than for the general population. Studies have estimated that depressive disorder occurs in 2–4% of persons in the community and in 5–10% of primary care patients [6].

A diagnosis of RA given has physical, psychological and socio-economic implications for the individual. From a psychological point of view, people with RA fear long-term pain, stiffness and fatigue. Most dread the development of joint deformities, especially of the hands. They have concerns about loss of function, work disability and the possible socio-economic effects of the disease. The potential toxicity of long-term treatment with disease modifying agents is also a worry.

Despite these rational fears and the major physical challenges that patients with RA face over many years, the majority do not develop depressive disorder. However, the significant proportion —perhaps as high as 1 in 5 to 1 in 10 out-patients— who do develop significant symptoms of depression carry a second heavy burden. Concomitant depression and RA disproportionately worsen many outcomes. Depression is linked with increased pain levels [3]. The causal relationship between pain and low mood most likely works in both directions [7, 8]. Comorbid depression has been shown to independently increase work disability in RA [9]. The loss of recreational and social activities in people with RA has been shown to significantly increase the risk of depressive symptoms [10]. The coexistence of both conditions adds to the burden of the disease on the health care system as well, with increased physician and general practitioner visits, increased pain complaints and more requests for analgesia. Depression can result in poor adherence to treatment.

Depression has been demonstrated to be an independent risk factor for mortality (non-suicide) in patients with RA [11]. This study by Ang *et al*. [11], involving 1290 patients with RA, showed that the cohort with persistent or recurrent depression over an initial 4 yr period had higher mortality rates than those without depression, when followed up over the subsequent 18 yrs.

Rates and patterns of suicide in patients with RA have also been studied. Timonen *et al* [12]. showed that 50% of their cohort of 19 patients with RA who had committed suicide were women, a much higher female percentage compared with the general population (18% in their study). About 90% of these women had suffered from comorbid depression. Treharne *et al*. [13] found that 11% of hospital out-patients with RA had suicidal ideation at one time; 30% of their patients with depression reported suicidal ideation.

Influences on the development of depression

There has been much discussion in the literature regarding the factors that influence the development of depressive symptoms in patients with RA. Disease activity alone does not equate with depressive symptoms reliably; many people with high levels of pain and disability do not report symptoms of depression [4]. Factors that have been purported to be influential include female gender [14], younger age at diagnosis [14] and personality traits such as low self-esteem, helplessness and avoidant (employing denial) coping [8, 15, 16]. Individuals vary greatly in their psychosocial acceptance of the diagnosis of RA, and poor adjustment to this diagnosis contributes to the onset of depressive symptoms [17]. It is recognized that rates of depression may be at least as high for patients recently diagnosed as for those with chronic RA [18]. Groarke *et al*. [17] found that illness perception had a greater effect than disease activity on the variance of pain in RA. They found that patients who perceived that the disease would last indefinitely, would have serious consequences, with little chance of cure or control, adjusted less well both physically and psychologically. Along with the recognition of the need to treat the physical aspects of the disease early [19, 20], the concept of a psychological 'window of opportunity' also exists [21]. It is during this time that positive attitudes can be fostered and negative coping mechanisms challenged, with benefits for long-term psychological health.

Depression and inflammation

From a biological viewpoint, research linking depression and inflammation is a growing field. In the Cardiovascular Health Study of over 4000 patients, a significant association was noted between high levels of C-reactive protein (CRP) and depression symptoms, even after adjusting for confounding factors [22]. Data from the ATTICA study [23] demonstrated high levels of CRP in people with depressive symptoms without any cardiovascular disease. Administration of cytokines including tumour necrosis factor-α (TNF-α) in animal and human studies has been shown to induce many symptoms of depression, including sleep disturbance, anorexia, loss of interest and mood disturbances [24]. As aforementioned, in RA studies, depression levels do not correlate well with disease activity levels as judged by standard clinical assessments or standard inflammatory markers such as CRP. However, there may be links to abnormal cytokine levels such as TNF-α, which have not been described to date. It may be that the use of biologic agents will influence the rate of depression in RA through their effects on the immune system as well as through the psychological benefits of physical remission.

Is depression in RA under-recognized?

Depression appears, therefore, to be a highly prevalent condition in our patients with RA and usually responds to treatment. However, it is estimated that only 30–50% of cases in the general population

receive appropriate intervention [25]. There are likely to be several reasons for this [25]. Patients are often reluctant to admit to feeling depressed on account of the perceived stigma of psychiatric illness. They often do not even admit it to themselves. Depression can be difficult to recognize and cannot be readily reduced to numbers as is the case with hypertension, T-scores and hyperlipidaemia. Rheumatologists and health care professionals may feel uncomfortable and lacking in the skills required for assessing depression. Many may feel that it is beyond their remit as physicians. This would not be surprising as neither the Irish nor the UK curricula for higher medical training (HMT) in rheumatology specifically include the skills of recognizing or managing depression. Those who do recognize symptoms may consider them as part of the illness and therefore acceptable, or see them as an adjustment to the condition that does not warrant therapy.

Management of depression in RA

Depression is an eminently treatable condition; 70% of the people with depressive disorder respond to first-line treatment [26]. There has been a major shift in the management of depression in recent times in that 9 out of 10 patients with depression are now treated in primary care alone [27]. Only selected refractory or severe cases require referral to a psychiatrist. Rheumatologists should similarly be involved as general practitioners are in managing this condition. Selective serotonin reuptake inhibitors (SSRIs), e.g. citalopram, sertraline and related drugs such as serotonin and noradrenaline reuptake inhibitors (SNRIs), e.g. venlafaxine are widely and successfully used to treat depression. They are safe to use, well-tolerated, have few side effects or interactions and are usually prescribed for defined treatment duration. Both the UK and Irish HMT curricula list knowledge of psychotropic medications as a requirement for trainees.

Psychological interventions in RA

Studies of psychological interventions, such as cognitive behavioural therapy (CBT), have shown that they can play an important adjunctive role in both newly diagnosed and chronic RA [26, 28]. CBT is a widely used form of psychotherapy, which aims to identify and change maladaptive patterns of thought and behaviour [29]. Specifically in physical illness, CBT can help patients adjust to their illnesses and acquire skills that can be used in their daily routine, improving the patient's sense of empowerment and control. CBT offered early in the course of RA [28] may produce long-term physical and psychological benefits, by preventing the development of negative illness perception and improving patients' sense of control of their disease. It is also of proven efficacy in managing depression in RA [26].

A typical course of CBT consists of 4–8 sessions, in either an individual or group setting [30] with a trained therapist. Some rheumatology departments do have access to a clinical psychologist to provide this service. Alternatively, a diploma in CBT can be obtained through a part-time study over a 1–2 yr period and could prove a viable option for rheumatology nurse specialists or occupational therapists. In daily practice, therefore, CBT has a validated role as an adjunctive therapy for treatment of depression in RA, and would also be of benefit for newly diagnosed patients who have a poor predicted psychological outcome, as judged by coping and personality assessment scores.

Other psychological interventions include patient education regarding 'self management' [31], which is increasingly being used in the management of chronic disease. In relation to RA, it aims to give patients control of their disease, by managing their own symptoms, maintaining physical function and coping with the psychological impact of living with a chronic condition. The concept of self-efficacy [32] seems to have a pivotal role in the success of a self-management programme; that is, the belief the patients have in their ability to successfully carry out tasks to achieve their targeted outcomes. Studies have shown that active self-management is associated with higher levels of adherence, and even if the ultimate target or therapy is ineffective, the process of striving for it leads to better outcomes for the patient [32]. Studies have shown that arthritis-specific self-management programmes lead to improved health outcomes including reduced rates of depression up to a year post-intervention [31, 33].

Improving awareness of depression in RA

As the treatments available to control RA have improved dramatically in recent years, there is much increased awareness of the need to prevent and treat common comorbidities, especially cardiovascular disease and osteoporosis. Depression is a symptomatic condition, in contrast to most of the natural history of other common RA comorbidities such as cardiovascular disease and osteoporosis. Depression appears to be common, and there is a need for greater recognition among rheumatologists of this relatively neglected condition. Also, there is a need for an acceptance of responsibility for identifying and managing it appropriately. How might this be achieved? The rheumatology HMT curriculum should include sessions from liaison psychiatrists and clinical psychologists during training days. Local and national meetings could include sessions on teaching skills in recognizing and treating depression. These would be of benefit to consultants and trainees, and would obviously be of use in managing other rheumatic conditions, fibromyalgia, for example. Consideration should be given to the acquisition of more specific psychological skills in rheumatology departments, by employing clinical psychologists and encouraging training in CBT by members of the multidisciplinary team.

In everyday practice, there should be an emphasis on providing good psychological support to those with newly diagnosed RA. In addition to information and education about RA, this includes reassurance about the efficacy of modern therapy and engendering a positive attitude. Rheumatologists and clinical nurse specialists have a particular responsibility here, as managing this period of adjustment may well have long-term benefits on coping mechanisms and reduce the risk of future depression [18, 21].

In established RA, rheumatology units should add screening for depression to their departmental guidelines. This could, for example, take the form of an annual or biennial assessment, again by the consultant or nurse specialist, coinciding with cardiovascular and osteoporosis risk factor screening. While structured questionnaires can be used, the majority of general practitioners and psychiatrists ask about typical symptoms such as low mood, loss of interest, anorexia, sleep disturbance and negative thoughts. They then make treatment decisions based on their clinical judgement. Those failing medical treatment are clearly more likely to become depressed and the changing of a disease modifying agent should automatically trigger an enquiry about mood by the rheumatologist.

Conclusion

In this era of biologic agents for the treatment of the physical aspects of RA, when rates of clinical remission are increasing, it must be expected that the rates of associated depression will decline. Deformity, disability and pain will be decreased. Turning off the inflammatory process early in the course of the disease should reduce depression, through immune mediated and/or psychological means. If, however, we fail to deal appropriately with early predictors of a poor psychological outcome, such as negative coping mechanisms and negative attitudes, then patients may continue to experience pain and depression in future years even when clinical remission is achieved. Those with established disease who have permanent joint damage, deformity and

disability will remain vulnerable to the developing depression. As a treatable condition with a high prevalence that causes significant suffering, we feel that a greater emphasis on recognizing and treating depression in RA is warranted.

Rheumatology	Key messages
	• Depression is a relatively common problem in RA. • There is a need for greater recognition among rheumatologists of depression and an acceptance of responsibility for identifying and managing it appropriately.

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