Rheumatoid arthritis (RA) is a chronic autoimmune disease that predominantly affects women. Several studies reported that therapy with second-line antirheumatic drugs must be started early if a beneficial effect on joint destruction is to be expected\(^1,2\). Delay in diagnosis by the physician may hamper early treatment\(^1,4\). Several studies have described differences between sexes in the use of medical services\(^3-8\). At the Department of Rheumatology of the Leiden University Medical Center, a special clinic for patients with arthritis of recent onset was established, the early arthritis clinic (EAC). Concerning the relevance of early treatment of patients with RA, we investigated if sex differences in referral also exist in RA patients in our EAC.

**MATERIALS AND METHODS**

*Patients.* The EAC was the only center for rheumatic patients in a semi-rural area with 300,000 inhabitants. The general practitioners (GPs) were motivated to refer patients if at least 2 of the following features were present: joint pain, joint swelling, and reduction of joint mobility. All patients referred to the special EAC by GP were seen within 2 weeks. Patients were accepted in the EAC if (1) arthritis was confirmed by a rheumatologist; (2) the history of symptoms lasted < 2 years; and (3) the patient had not seen a rheumatologist elsewhere for the same problem\(^9\).

Between 1993 and 1999, 142 female and 82 male consecutive patients who entered the EAC and fulfilled the ACR classification criteria for RA \(^2\) weeks after EAC entry were included in this report. Table 1 shows that both sexes were comparable. However, we observed a significant difference in the GP’s delay in referring female patients with RA to the EAC in comparison with male patients was observed (median of 93 days vs 58 days; \(p = 0.008\)).

**RESULTS**

Subsequently, the diagnosis of definite RA was made according to the 1987 American College of Rheumatology (ACR) criteria\(^10\), but without the requirement of a 6 week observation period of arthritis by a rheumatologist\(^6\).

A standard diagnostic investigation was performed at the first visit at the EAC, consisting of patient history (age, sex, patient’s medical encounter delay, family physician’s referral delay), physical examination [a joint tenderness score (Ritchie)\(^11\) and swollen joint score\(]\), laboratory examination [erythrocyte sedimentation rate (ESR) and rheumatoid factor (RF)], and radiological examination. The patient’s medical encounter delay was the time between onset of complaints and first medical encounter. The family physician’s referral delay was the time between the first medical encounter of the patient and the first visit to the EAC referred by the GP.

A total of 54 joints were assessed for soft tissue swelling, with a maximal swollen joint count of 22, since the metacarpophalangeal and proximal and distal interphalangeal joints at each side were counted as one joint. Also a disease activity score (DAS) was measured at the first visit\(^12\). The DAS is a composite index of disease activity that includes the number of painful joints, number of swollen joints, and ESR. It is used to monitor disease activity in RA patients in clinical trials. The formula of the DAS was as follows: \(DAS = 0.54 \times (\sqrt{\text{Ritchie score}}) + 0.065 \times (\text{number of swollen joints}) + 0.33 \times \ln \text{ESR} + 0.224\).

Statistical analysis. Differences between referral of men and women were tested with the Mann-Whitney U test. The test was 2 tailed and \(p < 0.05\) was considered significant.
patients were not referred to the EAC. Whether this differ-
ance in referral is also observed in other districts or coun-
tries has not yet been reported.

For some men and women, the GP’s referral delay was 6
months or longer. As several studies1,2 have shown that early
antirheumatic drug treatment of RA is more beneficial than
delayed treatment, the lack of early referral of these patients
is worrisome.

Drossaers-Bakker, et al14 found in their cohort of patients
with RA a nearly linear joint damage progression in the radi-
ographs of hands and feet (measured according to the Sharp
method15) of Sharp score 9 per year. We observed a statisti-
cally significant difference of 35 days in GP’s referral delay
between men and women. Thus a 5 week difference in initia-
tion of treatment means a possible difference of 0.9 Sharp
score, which may not be judged as relevant. However,
because of the pain and discomfort of the disease and
untreated disability that may interfere with work or function
at home, it may be desirable to refer patients earlier.

We observed that there is a significant delay in referral of
female patients to rheumatologists compared to male
patients with RA. Special educational programs to instruct
family physicians on the importance of early detection and
early referral of RA patients may be beneficial.

REFERENCES

comparison of combined step-down prednisolone, methotrexate and
sulphasalazine with sulphasalazine alone in early rheumatoid arthri-
suppression of inflammation in rheumatoid arthritis reduces
3. Chan KW, Felson DT, Yood RA, Walker AM. The lag time between
onset of symptoms and diagnosis of rheumatoid arthritis. Arthritis
and women in the rate of use of hip and knee arthroplasty. N Engl J
5. Katz JN, Wright EA, Guadagnoli E, Liang MH, Karlson EW,
Cleary PD. Differences between men and women undergoing major
orthopedic surgery for degenerative arthritis. Arthritis Rheum
107:19-25.
coronary artery disease treatment: gender bias or good clinical
9. van der Horst-Bruinsma IE, Speyer I, Visser H, Breedveld FC,
Hazes JM. Diagnosis and course of early-onset arthritis: results of a
special early arthritis clinic compared to routine patient care. Br J
10. Arnett FC, Edworthy SM, Bloch DA, et al. The American
Rheumatism Association 1987 revised criteria for the classification

### Table 1. Characteristics of 22 patients with RA.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Men, n = 82</th>
<th>Women, n = 142</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)*</td>
<td>59 (19–85)</td>
<td>57 (17–87)</td>
</tr>
<tr>
<td>Patient’s medical encounter delay (days)*</td>
<td>17 (0–396)</td>
<td>20 (0–482)</td>
</tr>
<tr>
<td>Family physician’s delay (days)*</td>
<td>58 (3–369)</td>
<td>93** (1–697)</td>
</tr>
<tr>
<td>RF positivity, %</td>
<td>58</td>
<td>59</td>
</tr>
<tr>
<td>DAS*</td>
<td>3.34 (1.62–5.77)</td>
<td>3.60 (1.61–6.07)</td>
</tr>
</tbody>
</table>

* Median (range). Differences were tested with the nonparametric Mann-
Whitney U test. ** p = 0.008.

