immune-mediated mechanisms have been suggested.[6 7] Furthermore, in Gambian children with malaria the titres of aPL are significantly higher in severe than in mild malaria.[3] However, a protective role of aPL has also been suggested. East African children with cerebral malaria had significantly lower titres of IgM anti-phosphatidylinositol antibodies than those with non-severe malaria.[4] This is possibly explained by the neutralisation of the pathogenic properties of parasite derived phospholipid.[8]

Whatever the pathogenic role of aPL, our present results indicate that acute *P falciparum* infection does not induce these antibodies in a white population. Whether aPL develop during chronic infections remains to be determined. Because genetic factors have been demonstrated to be associated with the prevalence of aPL,[9] it can be expected that people originating from malaria endemic areas are more prone to the induction of aPL. Therefore, analysis of aPL upon experimental infection with *P falciparum* in healthy volunteers from malaria endemic areas may further unravel the causal relation between malaria and aPL.

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Population based studies of biological antirheumatic drug use in southern Sweden: comparison with pharmaceutical sales

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This study aimed at assessing the drug costs for biological treatments in a geographically defined area in southern Sweden (Scania province, population 1 145 090, November 2002), and at identifying any geographical differences and changes with time in the overall use of these compounds. Also, we wanted to investigate the completeness of the registry held by the South Swedish Arthritis Treatment Group (SSATG).[1] During the study period no economic prescribing restrictions existed for these drugs in the region. The Swedish social security system covers all prescribed drug costs exceeding SEK 1800 (€170) a year to all patients in need, where need is based on their physician's judgment. Thus, the use of biological antirheumatic treatment was limited only by restricted drug availability and capacity of the administration facilities. Medical practice was, however, under strong influence by guidelines from the Swedish Rheumatological Association.

SSATG data were used to explore annual and regional relations, assessing the current and previous use of biological agents, prescription costs, and patient's diagnoses. The figures were adjusted according to the census population registry during 2000–03. Owing to legal constraints, which do not allow direct data linkage between SSATG and prescription databases, SSATG derived annual theoretical costs and sales of pharmaceutical agents to outpatients during the period 2000–03 (public domain) were broken down according to the patient's district of residency as the unifying concept. To obtain an estimate of the costs per week of using the different drugs we assumed the annual drug dosage to be 2550 mg etanercept, 2100 mg infliximab, 1040 mg adalimumab, and 36 500 mg anakinra, respectively. Year-specific pharmacy unit drug costs were used. In 2002 the resulting costs were SEK 144 935 (1 SEK = 0.1€) for etanercept, SEK 108 539 for infliximab, SEK 143 377 for anakinra, and SEK 112 895 for adalimumab. The estimated yearly consumption of etanercept and infliximab was based on a previous detailed health economic study,[2] whereas for anakinra and adalimumab we used the dosage recommended by the manufacturers. Registry data was checked against an assumed disease prevalence of 0.5% of the adult population.[3]

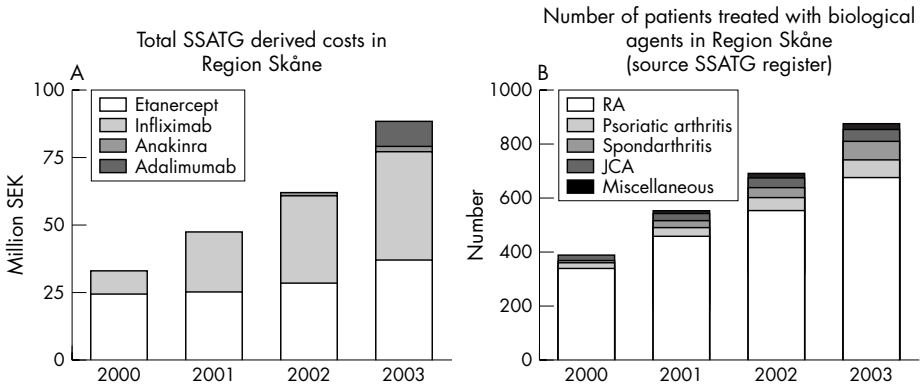

Figure 1 Total and drug related yearly biological drug costs (A) and number of patients treated with biological drugs related to the diagnosis (B) during 1999–2003 in Scania, derived from SSATG information.

Costs per head varied by a factor of 10 between residential districts, mostly because of low population numbers in some residential districts. However, when related to the five larger healthcare districts, twofold differences remained. The proportion of patients treated increased progressively and was about 14.9% of all patients with rheumatoid arthritis (RA) in 2003. The proportion of diagnoses other than RA increased from 13.1% to 22.7% during the study (fig 1). Pharmacy based and SSATG estimated cost ratios for all biological agents varied between 0.95 and 1.07 for the study years, but ratios for the individual drugs varied between 0.77 and 1.58. Concordance between pharmacy and SSATG cost figures increased with time (table 1), mostly explained by the increasing number of rheumatological centres joining the SSATG. The number of biological treatments started increased from 24 to 46 per 100 000 inhabitants between 2000 and 2003 and the number of biological treatments withdrawn increased from 4 to 20 per 100 000 inhabitants. The proportion of new biological treatments in patients previously treated with a biological drug increased from 4% to 44% between 2000 and 2003.

The regular overestimation of etanercept and underestimation of infliximab in SSATG costs suggests that the estimates have a systematic error. Several explanations can be offered, including annual pauses of longer than 1 week for etanercept, and prescription of infliximab for diagnoses other than those included in the SSATG registry. It can be estimated

Table1 Outward pharmaceutical sales and SSATG derived sales in SEK for biological drugs during the period 2000–03 in Scania (€1 = 9.05 SEK, $1 = SEK 8.5 SEK, May 2003)

	2000	2001	2002	2003	Sum 2000–03
Pharmacy					
Etanercept	18983353	23385102	25493373	34371270	102233098
Infliximab	13259906	27173845	37617778	43080718	121132247
Anakinra	0	0	1384760	2623048	4007808
Adalimumab	0	0	0	3999376	3999376
Total	*32243259*	*50558947*	*64495911*	*84074412*	*231372529*
SSATG					
Etanercept	24772571	25384933	28525854	37028082	115711440
Infliximab	8368944	21970848	32146426	40032834	102519052
Anakinra	0	0	950435	2026440	2976875
Adalimumab	0	0	0	4846806	4846806
Total	*33141515*	*47355781*	*61622715*	*83934162*	*226054173*
Pharmacy/SSATG cost ratio					
Etanercept	0.77	0.92	0.89	0.93	0.88
Infliximab	1.58	1.24	1.17	1.08	1.18
Anakinra			1.46	1.29	1.35
Adalimumab				0.83	0.83
Total	*0.97*	*1.07*	*1.05*	*1.00*	*1.02*
Proportion of adult population treated with biological agents (per 100 000 inhabitants)					
RA	38.3	51.4	61.4	74.6	
Psoriatic arthritis	2.3	3.6	5.2	7.3	
Other spondarthritis	1.1	2.8	4.6	7.6	
JCA	2.1	3.1	3.9	4.7	
Miscellaneous	0.2	1.1	1.6	2.3	
Total	*44.0*	*62.1*	*76.6*	*96.5*	
Proportion of patients with RA treated with biological agents (% of estimated RA population)					
	7.7	10.3	12.3	14.9	

For comparison the ratio between pharmaceutical and SSATG sales is also given. The proportion of patients for each diagnosis treated with biological agents as well as the relation (in %) to the estimated total RA population in Scania (0.5% of adult population) during the period 2000–03 according to the SSATG register.

(table 1) that the SSATG includes >90% of patients with arthritis currently treated with biological agents. This allows reliable continuous documentation of effects and potential side effects. Furthermore, a regional pharmacovigilance registry is also useful for assessing local differences in the use of the drugs and for evaluation of monitoring costs.

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Anti-cyclic citrullinated peptide antibodies in patients with rheumatoid arthritis treated with anti-tumour necrosis factor agents

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De Rycke *et al* pointed out the interesting discord between rheumatoid factor titre and the titre of anti-cyclic citrullinated peptide (anti-CCP) antibodies in their patients responding to infliximab plus methotrexate treatment.[1]

We have looked at 158 patients receiving either infliximab or etanercept plus methotrexate and treated for a slightly longer period over 1 year, all of whom, by definition, had responded with at least an ACR20, and in whom pretreatment serum samples were available.

We found essentially the same result for anti-CCP antibodies. Twenty four (15%) serum samples were negative at the outset, one of these became strongly positive in the serum specimen after 1 year. Of those who were strongly positive, one became negative; otherwise the titres remained relatively stable. Whether this in any way reflects the observation that the extra-articular features of rheumatoid arthritis—nodules, pulmonary disease, etc—do not seem to respond to these therapeutic agents might be a suggestion worth considering.

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