United Kingdom National Guideline on the Management of Sexually Acquired Reactive Arthritis 2008

Clinical Effectiveness Group (CEG)
British Association of Sexual Health and HIV (BASHH)

What is new in the guideline since the 2001 publication

Aetiology

- Rising incidence of spondyloarthropathies, including reactive arthritis, seen in association with HIV in sub-Saharan Africa but not in Caucasian populations.

Diagnosis

- Look for rectal gonococcal or chlamydial infection, if indicated by the sexual history.

Management

- Standard course antibiotic therapy should be used for any sexually transmitted infections (STIs) identified. The role of longer course and combination antimicrobial therapy for SARA remains unclear and there are no recommendations for its use.

- All individuals should be assessed and those at high risk of upper gastrointestinal complications should be offered a cyclo-oxygenase (COX) 2 selective drug, or a non-selective non-steroidal anti inflammatory drug (NSAID) combined with a proton pump inhibitor (PPI).

- COX 2 selective drugs, used long-term have been linked with increased cardiovascular risk and this may extend to all NSAIDs. Hence, treatment should be given for the shortest time period possible, at the lowest effective dose, and avoided or modified in at-risk patients.

- Biological agents (tumour necrosis factor (TNF) α blockers) are highly effective in the treatment of other spondyloarthropathies but their therapeutic role in SARA is not established. There are also concerns that they may re-activate the infective trigger.

- Updated information on treatment in pregnancy and breastfeeding.

Introduction and Methodology

Scope and purpose

The main objective is to reduce the number of sexually transmitted infections (STIs) and the complications that can arise in people either presenting with signs and symptoms of an STI, or undergoing investigation for possible infection, or with suspected reactive arthritis (ReA).

This guideline offers recommendations on the diagnostic tests, treatment regimens and health promotion principles needed for the effective management of sexually acquired reactive arthritis (SARA). It covers the management of the initial presentation, advice on referral where necessary, as well as how to prevent transmission of any detected infection and future triggering infections.

It is aimed primarily at people aged 16 years or older (see specific guidelines for those under 16) presenting to health care professionals, working in departments offering level 3 care in STI management (see national strategy[1]) within the United Kingdom. However, the principles of the recommendations should be adopted across all levels (levels 1 and 2 may need to develop, where appropriate, local care pathways).

Stake holder involvement

This guideline has been produced by medical specialists from relevant disciplines with input from specialist health advisors/nurses and a pharmacist. The guideline was pre-test piloted amongst a selection of intended end-users, formally and independently assessed by the CEG. Prior to publication the final draft of the guideline was placed on the BASHH website, and circulated through the BASHH regional network. After a period of three months any comments received were reviewed by the guideline authors, and acted on appropriately, before final authorisation by the CEG was given and publication was undertaken.

Rigour of development

An extensive literature review was performed using OVID and MEDLINE searches from 1966 to October 2007 using the keywords reactive arthritis, sexually acquired reactive arthritis, SARA, reiters, spondyloarthropathy, infectious arthritis.

The complete Cochrane library and National Institute for Health and Clinical Excellence was hand-searched in October 2007 for relevant documents.

Additional papers referenced by articles identified by the search strategy were also reviewed.

Aetiology

Reactive arthritis (ReA) is a sterile inflammation of the synovial membrane, tendons and fascia triggered by an infection at a distant site, usually gastro-intestinal or genital. ReA triggered by a sexually transmitted infection (STI) is referred to as sexually acquired reactive arthritis (SARA). This includes sexually acquired Reiter's syndrome, described as the triad of urethritis, arthritis and conjunctivitis, with or without other cutaneous or mucous membrane lesions such as, keratoderma blennorrhagica, circinate balanitis/vulvitis, uveitis, oral ulceration, cardiac or neurological involvement.

Most commonly lower genital tract infections, either urethritis or cervicitis, are associated with SARA with objective features of SARA being present in 0.8-4% of cases.[2-5] The place of upper genital tract infection, such as prostatitis and salpingitis, is unresolved. A rising incidence of spondyloarthropathies, including ReA, in association with the human immune deficiency virus (HIV) has been seen in sub-Saharan Africa, although this does not appear to be the case in Caucasian populations.[6-8]

The precise mechanisms linking infective agents with SARA are not clearly understood so links with specific micro-organisms are partly speculative.

- *Chlamydia trachomatis*, the commonest identifiable cause of non-gonococcal urethritis (NGU), has been the micro-organism most strongly linked to SARA being identified in 35-69% of cases, using non-nucleic acid amplification tests (NAAT).[3,9-14]

- *Neisseria gonorrhoeae* has been linked with up to 16% of cases, as distinct from its role in septic, gonococcal arthritis.[2,15-18] The precise role of this micro-organism in relation to SARA remains unknown.

- *Ureaplasma urealyticum* has been linked with a few cases and may be a cause of SARA in a minority.[19,20]

- A causal role for other genital tract pathogens and commensals is possible but there is currently insufficient evidence for evaluation.

Mechanisms of pathogenesis in SARA are not completely elucidated but appear to involve an immune response to uro-genital micro-organisms. DNA and/or surface antigens of *C. trachomatis*,[11,21-27] *U. urealyticum*,[26,28] and other mycoplasmas[29] may be detected within joint material from individuals with SARA. It is likely that the persistence of viable micro-organisms intra-articularly is an important factor in the causation and perpetuation of the arthritis. It has been shown in chlamydial infection that the organism persists in the synovium in an aberrant form with repressed synthesis of the major outer membrane protein (MOMP) and active production of heat shock protein (hsp), which contributes to the inflammatory response.[30,31]

SARA appears to occur over ten times more frequently in men compared to women, although under recognition in women may be a problem.[2,18,32,33] Possession of the HLA-B27 gene increases susceptibility to SARA by up to 50 fold.[3,5,10,13,16,32,34]

Clinical Features

History

- There may be a past or family history of spondyloarthritis or iritis.[2,5,17,33,34,35]

- Sexual intercourse, usually with a new partner, within 3 months prior to the onset of arthritis.[3,10,32]

Symptoms

- Onset of arthritis within 30 days of sexual contact in 88% of patients with a mean interval of 14 days between the onset of genital tract symptoms and arthritis. [2,3,17,32,33]

- A recent history of urethral discharge and/or dysuria in approximately 80% of men with SARA, although considerably fewer women are symptomatic.[10,12,17,18,32]

- Pain, with or without swelling and stiffness, at one or more (usually fewer than 6) joints, especially at the knees, ankles and feet.[5,14,17,32-34]

- Pain and stiffness at entheses, especially the posterior and plantar aspect of the heels, which often results in difficulty

in walking. Enthesitis and/or fasciitis occurs in up to 40% of patients.[2,14,16,18,32,33]

- Painful movements may also result in 30% from tenosynovitis and in 16% painful swelling of a toe or finger (dactylitis) may occur.[14,32,33]

- Low back pain and stiffness is common in the acute episode and sacro-iliitis occurs in approximately 10% of patients during the acute episode.[2,14,16-18,32,33,36,37]

- Irritable eyes, with or without redness, photophobia or a reduction in visual acuity. Conjunctivitis occurs in 20-50% of patients with SARA, often bilateral and preceding the arthritis by a few days, but iritis is less common occurring in around 2-11% of patients.[2,5,16-18,32,33,37] Other eye lesions occur rarely.[2,16,18]

- Systemic symptoms of malaise, fatigue and fever occur in approximately 10% of patients.[32,34]

Signs

- Genital infection. Manifest in men by urethritis, urethral discharge and/or epididymo-orchitis and in women by muco-purulent cervicitis, with or without easily induced cervical bleeding, and/or abdominal pain. Infection may be asymptomatic, particularly in women.[10,12,17,18,32]

- Arthritis, almost invariably affecting 1-5 lower limb joints in an asymmetrical distribution. Persistent small joint involvement may be erosive. Upper limb involvement is rare in the absence of psoriasis.[5,17,32-34]

- Enthesopathy. Tenderness, with or without swelling at the sites of tendon or fascial attachments, especially the Achilles tendon and plantar fascia attachments to the calcaneum.[2,5,16,18,32,33]

- Tenosynovitis. Tenderness, with or without swelling over tendon sheaths and crepitus on movement. Classical dactylitis may be seen.[32,33]

- Pain on direct sacral pressure may indicate acute sacro-iliitis.[2,16,18,32,33] Care should be taken to distinguish this from lumbosacral disc disease or other pathology.

- Pain and redness of the eye is usually due to conjunctivitis, or rarely iritis.[2,5,16-18,32,33,37] Slit lamp examination is essential to differentiate them. Rarely, corneal ulceration, keratitis and intra-ocular haemorrhage may be seen and optic neuritis and posterior uveitis have been described.[2,5,16,18,33]

- Psoriasiform rash which may be typical plaque or guttate cutaneous psoriasis in 12.5%,[17] nail dystrophy in 6-12%,[17,37] typical lesions of psoriasis on the glans penis or labia (but there may also be erosive circinate balanitis or vulvitis) in 14-40%,[2,13,16,18,32,33,37] tongue (geographical tongue) in about 16%,[37] or pustular psoriasis on the soles of the feet (keratoderma blennorrhagica) in up to 33%.[2,5,13,16-18,32,33,37] The latter may rarely occur on the palms of the hands. Stomatitis and oral ulceration occur in approximately 10%.[13,16-18,33]

- Heart lesions are almost invariably asymptomatic although tachycardia, left ventricular dilatation, and rarely pericarditis and aortic valve disease may occur. Electrocardiographic abnormalities, including conduction delay, are recorded in 5-14% of patients.[13,16-18,33,38]

- Renal pathology, such as proteinuria, microhaematuria and aseptic pyuria, is seen in about 50% and is usually asymptomatic. Glomerulonephritis and IgA nephropathy rarely occur.[34,39]

- Rare manifestations include thrombophlebitis of the lower limbs, subcutaneous nodules, nervous system involvement including meningoencephalitis and nerve palsies.[2,17,18,33]

- Fever and weight loss occur in a minority of patients, approximately 10%.[14,32,34,36]

<u>Complications</u>

In the majority of individuals with SARA the disease is self-limiting with a mean first episode duration of 4-6 months followed by full recovery.[2,5,14,32,33,37] Approximately 50% have recurrent episodes at variable intervals.[2,5,17,33,35] The complications of SARA are principally due to aggressive arthritis and are more likely if the individual possesses the HLA-B27 gene.[5,13,16,32,40]

- Chronicity with symptoms persisting for more than one year in approximately 17% of patients.[33]

- Erosive joint damage especially affects the small joints of the feet with 12% exhibiting foot deformities, although severe deformity is rare.[2]

- Persistent locomotor disability occurs in approximately 15%, due principally to erosive damage with deformity of the metatarsophalangeal, ankle or knee joints, or as a consequence of sacro-iliitis or spondylitis.[16,35] Heel and foot involvement is particularly associated with subsequent disability. No accurate estimates of the prevalence of ankylosing spondylitis are available although it has been described in up to 23% of patients with severe disease and sacro-iliitis has been reported in 37% of patients over a 15 year follow up period.[14,36] It is unclear whether the development of ankylosing spondylitis is a complication of the ReA or the independent development of two conditions in the same genetically predisposed population.

- Inadequately treated, or recurrent, acute anterior uveitis may lead rapidly to cataract formation and blindness in a minority.[16-18,35]

Diagnosis

The diagnosis of SARA involves three components.

- Recognition of the typical clinical features of spondyloarthropathy.

- Demonstration of evidence of genito-urinary infection by the identification of: -

    - Urethritis in men. Urethral discharge, dysuria and/or epididymo-orchitis may be present. Asymptomatic cases with *C. trachomatis* are relatively common, occurring in up to 50% of men. Microscopic confirmation is by a Gram stained urethral smear demonstrating >= 5 polymorphonuclear leucocytes (PMNLs) per high power (x1000) microscopic field (averaged over five fields with the greatest concentration of PMNLs), and/or >= 10 PMNLs per high power (x1000) microscopic field on a Gram stained preparation from a centrifuged sample of a first void urine (averaged over five fields with the greatest concentration of PMNLs).

    - Muco-purulent cervicitis in women. Post coital or intermenstrual bleeding, dysuria, purulent vaginal

discharge, purulent or muco-purulent endocervical exudate, with or without easily induced cervical bleeding, and/or lower abdominal/pelvic pain may be present. However, cervical infection with *C. trachomatis* is frequently asymptomatic, occurring in about 70% of women.

- Rectal infection in men and women. This may present with anal discharge and/or anorectal discomfort due to proctitis but most infections are asymptomatic.

- The identification of genital pathogens, particularly *C. trachomatis* or *N. gonorrhoeae*. Full screening for STIs is essential from sites, as indicated by the sexual history.

- Please refer to the relevant UK guidelines on NGU, *C. trachomatis,* gonorrhoea, and to the UK guidelines on screening and testing for STIs.[41]

- Investigation of specificity and activity of arthritis.

Management

General advice

The principles of management are governed by the expectation that SARA is a self-limiting disease in the majority of patients.

Patients should be advised to avoid sexual intercourse (including oral sex) until they and their partner(s) have completed treatment and follow-up for any genital infection identified.

Patients should be given a detailed explanation of their condition with particular emphasis on the long-term implications for the health of themselves and their partner(s).

This should be reinforced by giving them clear and accurate written information.[13,42]

Further investigation

The following investigations are essential, often useful or sometimes useful.[5,9,13,14,16-18,32-34,35-37,42-46] Genito-urinary medicine (GUM) specialists are advised to liaise with and/or refer to other specialists including rheumatologists, ophthalmologists and dermatologists for all patients with

significant involvement of extra-genital systems. It is advised that all patients with SARA are referred to an ophthalmologist, if possible, for slit lamp assessment. Essential investigations should be performed by GUM specialists whilst other investigations are suggested following appropriate referral.

Essential

Full screening for STIs, including HIV.
Acute phase response such as, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), or Plasma viscosity (PLV).
Full blood count (FBC).
Urinalysis.

Investigations, which are often useful

Liver and kidney function tests.
HLA-B27.
X-rays of affected joints and sacro-iliac joints.
Electrocardiogram.
Echocardiogram.
Ophthalmic evaluation including slit lamp assessment.

Investigations, which are sometimes useful

Blood cultures.
Stool culture (if enteritic ReA is suspected).
Serology specific for *C. trachomatis.*
Ultrasonography of affected joints or entheses.
Magnetic resonance imaging of sacro-iliac joints.
Synovial fluid analysis for cell count, Gram stain, crystals, culture.
Synovial biopsy.
Exclusion tests for other diseases with rheumatological features, for example, rheumatoid factor (rheumatoid arthritis), autoantibodies (systemic lupus erythematosus), plasma urate (gout), chest X-ray and serum angiotensin-converting enzyme (ACE) level (sarcoidosis).

Treatment

Treatment is directed at several distinct elements of the condition. It is advisable that advice/assessment is obtained from relevant specialists as indicated above.

Constitutional symptoms

- Rest.
- Non steroidal anti-inflammatory drugs (NSAIDs).

Genital infection

- Antimicrobial therapy for any genital infection identified should be as in uncomplicated infection. Please refer to the relevant infection guidelines.[41] Whether short course antibiotic treatment of the acute genital infection influences the non-genital aspects of SARA is controversial, with the probability being that it does not once the arthritis is manifest. (Ib, A) [32,37,47,48]

Arthritis

First line therapy

- Rest with the restriction of physical activity, especially weight bearing activity where leg joints are involved. Balance with the use of physiotherapy to prevent muscle wasting. Physiotherapy and exercise are particularly important where there is axial involvement. (IV, C) [5,31,34,42,49-52]

- Physical therapy with the use of cold pads to alleviate joint pain and oedema. (IV, C) [49-51]

- NSAIDs are well established as efficacious agents in many inflammatory arthritides and form the main stay of therapeutic management. It is important that they are used regularly to achieve the maximum anti-inflammatory effect. There is no definite drug of choice and the individual response varies between individuals. (IIb, B) [5,13,14,34,42,49-51,53-56]

  NSAIDs have significant gastrointestinal, renal and cardiovascular side effects. All individuals should be assessed and a cyclo-oxygenase (COX) 2 selective drug should be used for those at high risk of upper gastrointestinal complications, such as gastrointestinal bleeding. Adding gastro-protective agents, such as misoprostol, histamine-2 blockers and a proton pump inhibitor (PPI), to non-selective NSAIDs can also reduce the gastrointestinal risks. COX-2 selective drugs, used long-term have been linked with increased cardiovascular risk and this may extend to all NSAIDs. Therefore, treatment should be given for the shortest time period possible and avoided or modified in at-risk patients. (1a, A) [5,42,53,57-59]

- Intra-articular corticosteroid injections, especially valuable for single troublesome joints. They may also be used for inflamed sacro-iliac joints. Proven value in other inflammatory arthritides but there are no randomised placebo-controlled trials (RPCTs) of its use in SARA. (IV, C) [5,13,14,34,42,49,51,59,60-63]

<u>Second line therapy (moderate/severe arthritis/failure of first line</u>)

- As above +

- Systemic corticosteroids. If used, consideration should be given to anti-osteoporosis prophylaxis. (1a, A) [66-67] Corticosteroids are valuable where severe symptoms arise from several joints, often in the presence of constitutional illness, either as a short course of oral prednisolone 10-30mg daily or as a single intramuscular dose of depot methyl prednisolone 80-120mg. In rheumatoid arthritis it has been shown to suppress inflammation but there are no RPCTs of its use in SARA. (IV, C) [5,34,49,42,64]

- Sulphasalazine. Indicated where disabling symptoms persist for 3 or more months, or evidence of erosive joint damage is present. Sulphasalazine reduces the severity and duration of peripheral joint synovitis but probably does not influence ultimate recovery. There may also be some benefits in early sacroiliitis but not in established ankylosing spondylitis. High doses, 3g daily, are associated with significant toxicity, especially gastrointestinal, which may necessitate cessation of treatment, whereas 2g daily appears equally effective and better tolerated. (Ib, A) [13,34,49,59,68-72]

- Methotrexate. Indicated where disabling symptoms persist for 3 or more months, or evidence of erosive joint damage is present. Doses range from 7.5-15mg orally as a single weekly dose. Oral folic acid should be given, usually as a single 5mg dose weekly, with or on the day following the methotrexate dose. Methotrexate is favoured by many physicians because of the ease of weekly oral administration and the favourable responses seen in rheumatoid disease and psoriatic arthritis. There are no

published RPCTs of its use in SARA. (IV, C) [5,13,34,42,49,50,59,73]

- Azathioprine. Indicated where disabling symptoms persist for 3 or more months, or evidence of erosive joint damage is present. Doses of 1-4mg/kg/body weight per day may be used. (III, B) [13,34,49,59,74]

- Gold salts and D-penicillamine. These drugs are occasionally used when persistent polyarthritis is present. No RPCTs have been published concerning their use in SARA. (IV, C) [13,34,49]

- Biological agents. Tumour necrosis factor (TNF) α blockers, such as infliximab, etanercept and adalimumab, are highly effective in the treatment of rheumatoid arthritis,[58,75-78] ankylosing spondylitis, [31,40,52,58,78-83] psoriatic arthritis,[31,40,52,58,78,81,83,84-86] and other spondyloarthropathies.[59,81,87,88]

  There are side effects with TNF α blockers including infusion reactions; an increased risk of infection, including tuberculosis; development of autoantibodies; systemic lupus erythematosus and vasculitis; demyelinating disease; and worsening congestive cardiac failure. It is not known whether there is a long-term increased risk of malignancy in patients with spondyloarthropathies.[59,78,79,81,89,90]

  Experience of the use of biological agents in the treatment of ReA, including SARA, is essentially anecdotal. It is possible that they may re-activate the infective trigger in patients with ReA. The place of such therapy in SARA is therefore not yet established. (IV, C) [5,13,31,59,81,91-95]

  Antibiotics

  - Short course antibiotic therapy used for the treatment of concomitant uro-genital infection may reduce the risk of recurrent arthritis developing in individuals with a history of ReA but otherwise there is little evidence of benefit in respect of the duration, severity or course of the arthritis. (Ib, A) [14,32,37,47,48]

  - Longer course antibiotic therapy has been considered. However, many studies have had

small numbers of individuals with SARA and in the main antibiotic therapy has been commenced after the arthritis has established. Antibiotics may also have anticollagenolytic properties.[96] Conflicting results have been obtained, with one study by Lauhio et al identifying that lymecycline given for 3 months reduced the duration of arthritis in *C. trachomatis* triggered SARA.[97] However, no significant effect was seen in placebo-controlled studies of three month courses of ciprofloxacin, azithromycin, or doxycycline, a twelve month course of ciprofloxacin, nor in placebo-controlled comparative studies of short course versus 4 months of doxycycline therapy.[98-104]

Combination antimicrobial therapy for a three month period has been investigated with significant improvements in arthritis and back pain being reported in those treated with doxycycline and rifampicin compared with doxycycline alone.[105] Others have shown no benefit in a combined placebo controlled study with ofloxacin and roxithromycin.[106]

The effect of longer term therapy on the late prognosis of arthritis has been evaluated. One study has shown that 8% of those treated with a three month course of ciprofloxacin, compared to 41% in a placebo group, had developed chronic disease when assessed 4-7 years later.[107] However, this has not been confirmed by a ten year follow-up study of patients treated with lymecycline, despite the benefits seen initially.[108]

- The role of combination or longer term antimicrobial therapy in SARA is not yet established and further studies are needed. A Cochrane systematic review is currently underway to evaluate this contentious area. (Ib, A) [5,14,52,97-110]

- Medical synovectomy using Yttrium-90, osmic acid, Samarium-153 or Rhenium-186. All have been shown to have short term benefit in chronic mono-articular synovitis. Advantages over intra-articular corticosteroid injections have not been confirmed. (Ib, A) [61,111]

- Surgery. Exceptionally, surgical treatment including synovectomy and arthroplasty, is valuable. For synovectomy the concomitant use of azithromycin for three months has been suggested but the study describing this did not include a placebo arm so a definitive benefit could not be confirmed.[49,112]

Enthesitis

- Rest. (IV, C) [34]
- Physiotherapy and ultrasound. [31]
- Orthototics with insoles, cushioning and heel supports. (IV, C) [5,31]
- NSAIDs, usually oral but occasionally may be useful topically. (IV, C) [5,31.34,59]
- Local corticosteroid injection. (IV, C) [14,31,51,61,62]
- Radiotherapy for persistent disabling heel pain, exceptionally.[31]
- Surgery, exceptionally.
- TNF blockers appear to improve enthesitis associated with other spondyloarthropathies but there are no RPCTs of its use in SARA. (IV, C) [83,85]

Mucous membrane and skin lesions

- No treatment for mild lesions.
- Keratinolytic agents, such as topical salicylic acid ointments or corticosteroid preparations, in mild to moderate cases. Low potency topical corticosteroids are the best option for mucosal sites. (IV, C) [13,34]
- Vitamin D3 analogues in mild to moderate cases. Calcitriol ointment is better tolerated in flexural sites than calcipotriol. The ointment preparation of calcipotriol has been withdrawn and is no longer available but the cream formulation can still be obtained. (IV, C) [113]
- Methotrexate, if severe lesions. (IV, C) [13,34,73]
- Retinoids, such as acitretin, if severe lesions. (IV, C) [13,34,114]
- TNF blockers, such as infliximab and etanercept, have been effective for psoriatic skin lesions but no RCPTs have been performed in SARA. (IV, C) [52,78,81,83-86]

Eye lesions

- Should be managed with ophthalmological advice.

- Slit lamp assessment is essential to diagnose uveitis, which if untreated may result in irreversible visual loss. Therapy for uveitis consists of corticosteroid eye drops or oral corticosteroids, and mydriatics, although posterior uveitis usually requires more aggressive treatment. Limited information is available on the use of TNF blockers for uveitis, although they have been reported to reduce the frequency of episodes of uveitis when treating ankylosing spondylitis. Their therapeutic role is not yet known. (IV, C) [34,78,81,83,115-118]

Post-inflammatory pain and fatigue

- Explanation and patience.
- Low dose tricyclic drugs, such as amitriptyline 10-25mg at night, if severe symptoms.

Prophylaxis

- In addition to the advice to avoid sexual intercourse (including oral sex) until they and their partner(s) have completed treatment and follow-up for any genital infection identified, patients should be advised to avoid potentially 'triggering infections' in the future, either uro-genital or enteric. Hence, safer sexual practice should be discussed and the importance of food hygiene stressed.

Pregnancy and breastfeeding

- All medications should be avoided during pregnancy and breastfeeding where possible.
- Antibiotics. Please refer to the relevant infection guidelines.[41]
- NSAIDs may potentially produce sub-fertility as a result of the leuteinised unruptured ovarian follicle syndrome.[119] NSAIDs, used regularly during pregnancy, may produce premature closure of the foetal ductus arteriosus, oligohydramnios, delayed onset and increased duration of labour.[120,121] Advice regarding breastfeeding depends on the specific NSAID being used.[121]
- Corticosteroids are low risk but with prolonged use in pregnancy there is a risk of intrauterine growth restriction and foetal adrenal suppression. Systemic effects in the breastfeeding infant are unlikely if the maternal dose of prednisolone is less than 40mg

daily. Adrenal function should be monitored in the breastfeeding infant if higher doses are used.[121]

- Sulphasalazine appears to have only small theoretical risks but should be used with caution in pregnancy and breastfeeding. It may induce oligospermia in men.[121]
- Azathioprine appears to be safe during pregnancy but should not be initiated during pregnancy, if possible. It should be discontinued if breastfeeding.[121]
- Methotrexate and retinoids are teratogenic and contraindicated during pregnancy and breastfeeding. Both men and women using methotrexate should avoid conception during drug taking and for at least 3 months after. Women using retinoids, such as acitretin, should be advised to use effective contraception for at least one month before treatment, during treatment, and for at least 2 years after stopping treatment (oral progestogen-only contraceptives are not considered effective).[121]
- Gold salts should be avoided during pregnancy and breastfeeding. With the oral preparation effective contraception should be used during and for at least six months after treatment.[121]
- TNF blockers should be avoided during pregnancy. Women should be advised to use adequate contraception during treatment and with adalimumab and infliximab this should be continued for 5 and 6 months, respectively, after the last dose. Breastfeeding should be avoided for up to 6 months after the last dose. [121]

Sexual partners

- Partner notification, treatment, and the contact tracing period is dependent on the genital infection identified. Please refer to the relevant infection guidelines.[41]

Follow-up

- GUM follow-up is dependent on the genital infection identified. Please refer to the relevant infection guidelines.[41]
- Extra-genital manifestations should be followed up under the direction of the relevant specialist.

Qualifying statement

The recommendations in this guideline may not be appropriate for use in all clinical situations. Decisions to follow these recommendations must be based on the professional judgement of the clinician and consideration of individual patient circumstances and available resources.

All possible care has been undertaken to ensure the publication of the correct dosage of medication and route of administration. However, it remains the responsibility of the prescribing physician to ensure the accuracy and appropriateness of the medication they prescribe.

Auditable Outcome Measures

- A sexual history should be taken, particularly covering the last three months (target 100%).
- A full screen for STIs, including an HIV test, should be offered (target 100%).
- Patients should have an ESR, CRP or PLV measured (target 100%).
- Patients should have a FBC performed (target 100%).
- Urinalysis should be performed in all cases (target 100%).

- Appropriate antibiotic therapy for any genital infection identified should be prescribed as detailed in the relevant guidelines (target 100%).[41]
- Partner notification rate, according to gonorrhoea and *C.trachomatis* guidelines, where an STI is identified.[41]
- Prevention of recurrent genital infection.

- Patients prescribed an NSAID should have a documented prior assessment of risk for gastrointestinal complications (target 100%).
- Patients prescribed an NSAID should have a documented prior assessment of cardiovascular risk (target 100%).

- Duration of inability to work (target 80% 6 months or less).
- Need for admission to hospital (target less than 10%).
- Duration to full recovery (target 80% 6 months or less).
- Presence of erosive joint damage (target 20% or less).
- Presence of long-term disability (target 20% or less).

- Patients with significant extra-genital involvement should be referred to the appropriate specialist (target 100%).

- Patients should receive a detailed verbal explanation of their condition (target 100%).

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