RA, pregnancy and antirheumatic drug exposure

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RA

The first reports about spontaneous improvement of RA during pregnancy and its flare after pregnancy date back to the 1930s.

(Mayo Clin Proc 1938;13:161–167)

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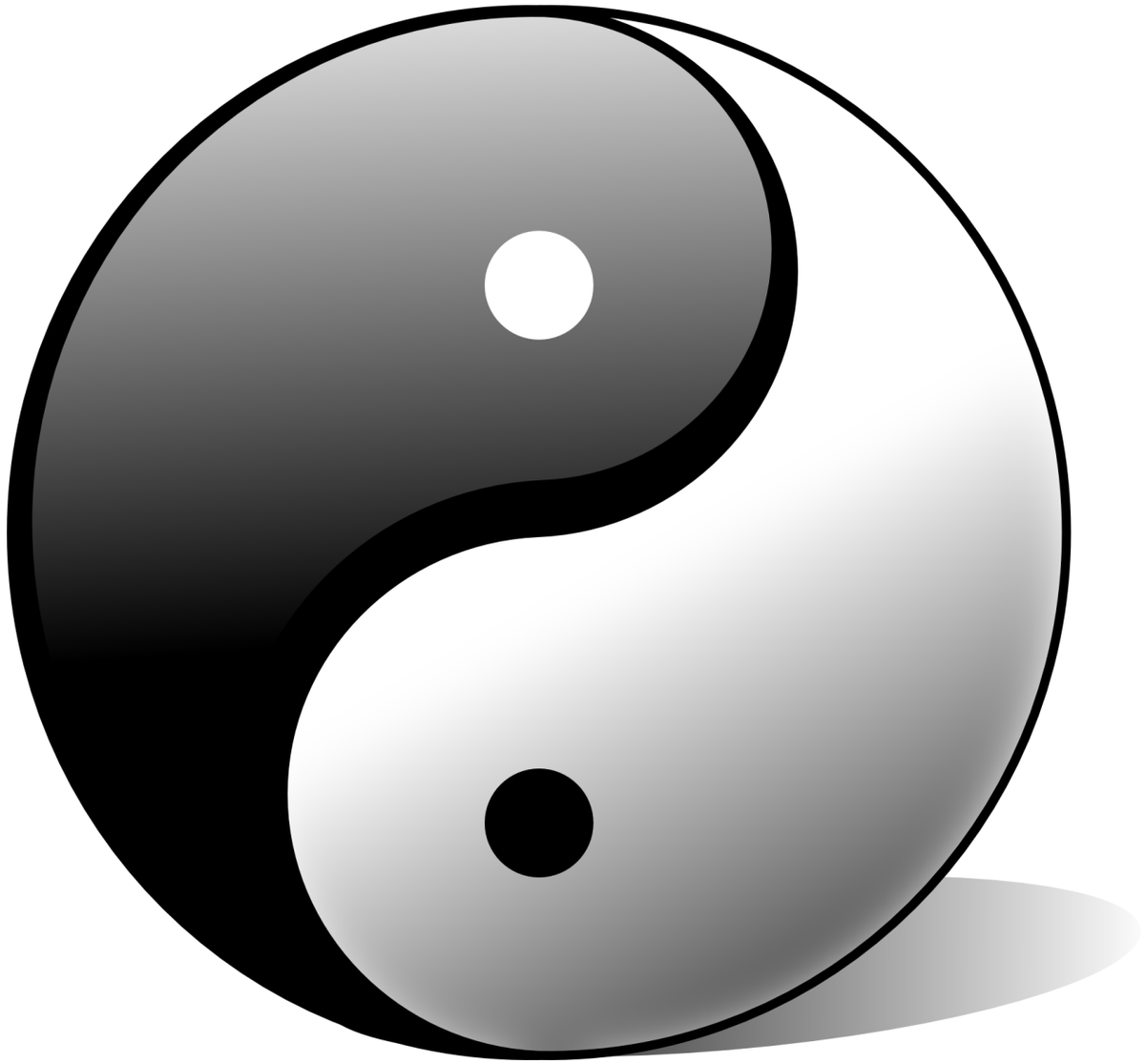

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Disease activity can adversely affect pregnancy (e.g. outcome preterm, delivery lower birth weight)

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RA

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Disease activity can adversely affect pregnancy (e.g. outcome preterm, delivery lower birth weight)

A decrease of disease activity is observed in about 50% of women. The improvement may occur more frequently in absence of anti-CCP and RF

de Man YA ARD 2009, COR 2014

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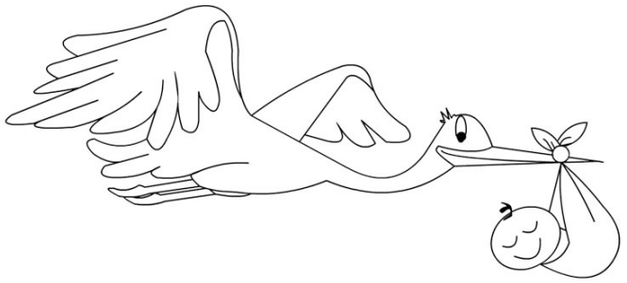
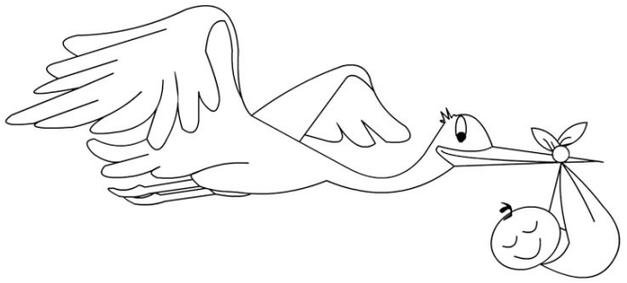
- With new effective therapies and less long-term disability most women can contemplate pregnancy
- The number of RA patients experiencing a pregnancy has significantly increased over the last 20 years, though substantial risk for adverse maternal and fetal outcomes remain

- A desire for children or the presence of pregnancy limits the drug therapy options for a woman with RA and therapy must be tailored for the individual patient
- Adjustment of therapy in these patients aims to use medications that support disease control in the mother and are considered safe for the fetus.



- ☐ Pregnancy planning
- ☐ Antirheumatic drugs in pregnancy
- ☐ Antirheumatic drugs during lactation
- ☐ Unplanned pregnancy
- ☐ Paternal exposure
- ☐ Follow up of children



- ☐ Pregnancy planning

The EULAR points to consider for use of antirheumatic drugs before pregnancy and during pregnancy and lactation

Overarching principles

A. Family planning should be addressed in each patient of reproductive age and adjustment of therapy considered before a planned pregnancy.

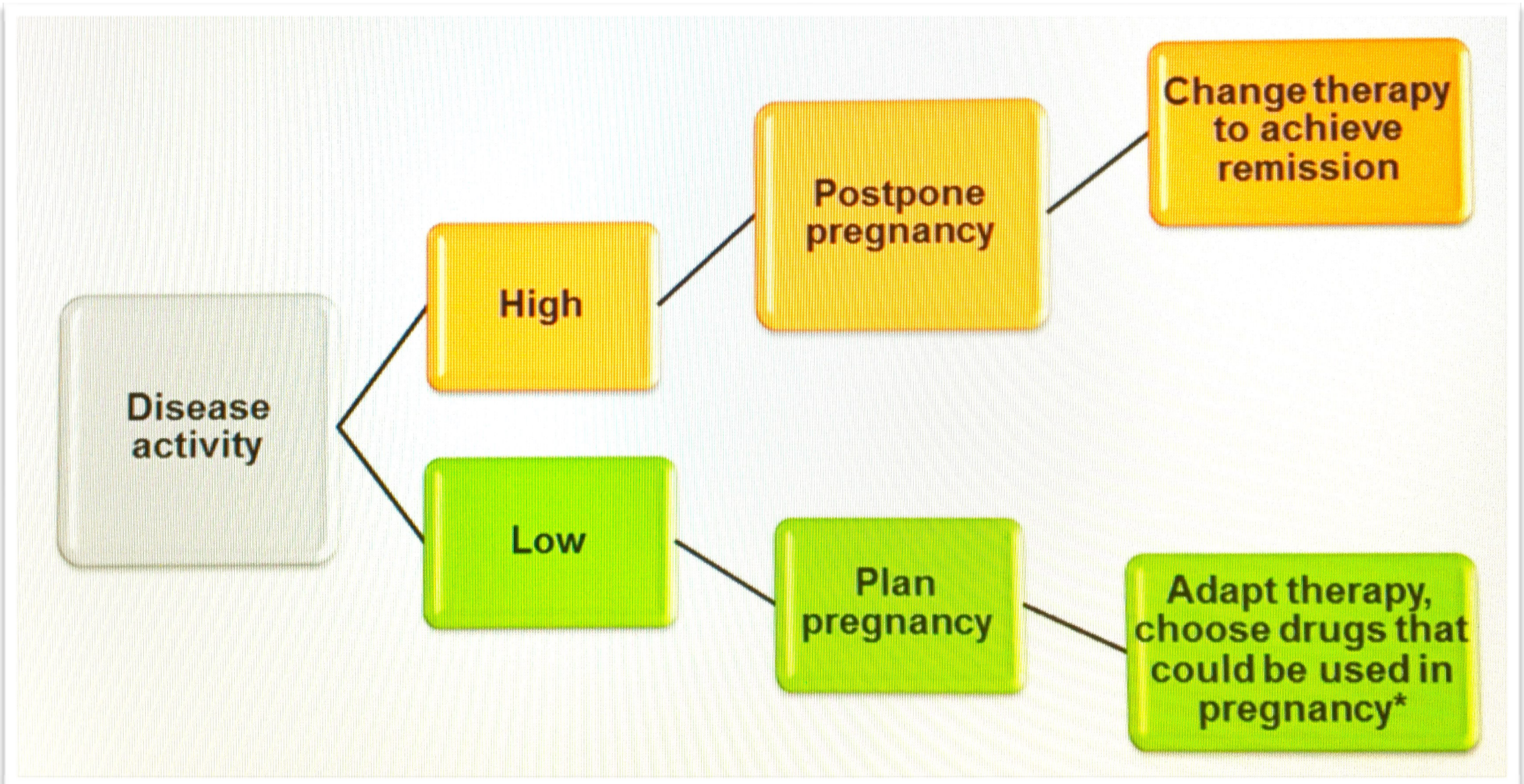
B. Treatment of patients with rheumatic disease before/during pregnancy and lactation should aim to prevent or suppress disease activity in the mother and expose the fetus/child to no harm.

C. The risk of drug therapy for the child should be weighed against the risk that untreated maternal disease represents for the patient and the fetus or child.

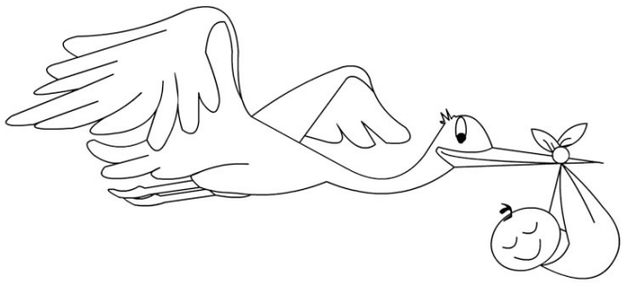
D. The decision on drug therapy during pregnancy and lactation should be based on agreement between the internist/rheumatologist, gynaecologist/obstetrician and the patient, and including other healthcare providers when appropriate

Götestam Skorpen C, *et al*. *Ann Rheum Dis* 2016;**0**:1–16.

Strategy for pregnancy planning

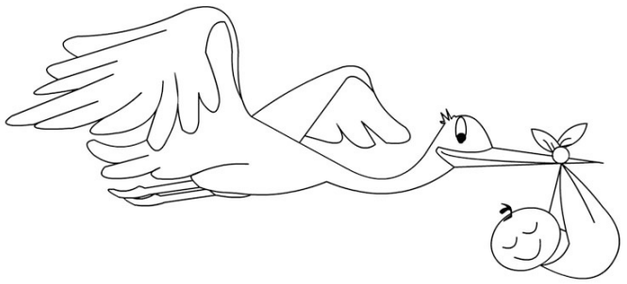


Adjustment of therapy for pregnancy planning



☑ Pregnancy planning

Management of RA during pregnancy and lactation requires weighing risks of withholding treatment from the mother against any risk to the fetus/child via exposure to drugs during pregnancy or breast feeding



☑ Pregnancy planning

Management of RA during pregnancy and lactation requires weighing risks of withholding treatment from the mother against any risk to the fetus/child via exposure to drugs during pregnancy or breast feeding

☐ Antirheumatic drugs in pregnancy

Points to consider for use of anti rheumatic drugs in pregnancy

csDMARDs

Grade of recommendation

csDMARDs proven **compatible** with pregnancy are **hydroxychloroquine, chloroquine, sulfasalazine, azathioprine, ciclosporin**. They should be continued in pregnancy for maintenance of remission or treatment of a disease flare.

Consensus on statements and expert opinion

Drug	Statement on compatibility of drug with pregnancy based on evidence	Percentage of agreement with statement	Expert opinion on use of drug in clinical practice*
Hydroxychloroquine	Current evidence indicates no increased rate of congenital malformations Hydroxychloroquine can be continued throughout pregnancy	100	
Chloroquine	Current evidence indicates no increased rate of congenital malformations Chloroquine can be continued throughout pregnancy	100	
Azathioprine	Current evidence indicates no increased rate of congenital malformations Azathioprine can be continued at doses up to 2 mg/kg/day throughout pregnancy	100	
Sulfasalazine	Current evidence indicates no increased rate of congenital malformations Sulfasalazine can be continued at doses up to 2 g/day with concomitant folate supplementation throughout pregnancy	100	
Ciclosporin	Current evidence indicates no increased rate of congenital malformations Ciclosporin can be continued throughout pregnancy at the lowest effective dose	100	

*As an expert in the field.
I would recommend the drug in the same way as if the patient was not pregnant.
I would only recommend the drug if I feared at least moderate disease activity in its absence.
I would only recommend the drug if I feared at least severe disease activity in its absence.
I would never recommend the drug in pregnancy.

B Category II evidence from at least one controlled study without randomisation (2A) or from at least one type of quasi-experimental study (2B), or extrapolated recommendations from category I evidence.

Götestam Skorpen C, *et al. Ann Rheum Dis* 2016;**0**:1–16.

Points to consider for use of anti rheumatic drugs in pregnancy

csDMARDs

Grade of recommendation

csDMARDs **methotrexate, mycophenolate mofetil and cyclophosphamide** are **teratogenic** and should be withdrawn before pregnancy.

Consensus on statements and expert opinion

Drug	Statement on compatibility of drug with pregnancy based on evidence	Percentage of agreement with statement	Expert opinion on use of drug in clinical practice*
Methotrexate	Current evidence indicates an increased rate of congenital malformationsIn a planned pregnancy, methotrexate should be withdrawn 1–3 months before pregnancy	100	
Cyclophosphamide	Current evidence indicates an increased rate of congenital malformations Cyclophosphamide must be withdrawn before a planned pregnancy	100	
Cyclophosphamide	The use of cyclophosphamide might be justified to treat life-threatening conditions in the second and third trimesters	100	

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I would recommend the drug in the same way as if the patient was not pregnant.
I would only recommend the drug if I feared at least moderate disease activity in its absence.
I would only recommend the drug if I feared at least severe disease activity in its absence.
I would never recommend the drug in pregnancy.

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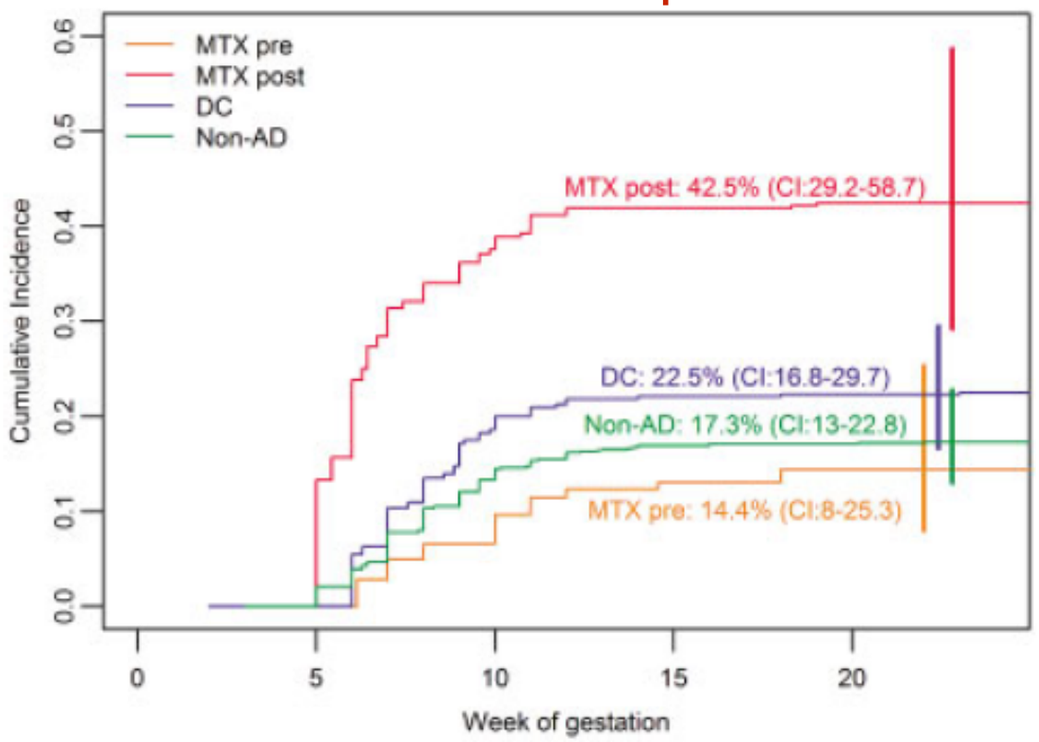
Pregnancy Outcome After Methotrexate Treatment for Rheumatic Disease Prior to or During Early Pregnancy

A Prospective Multicenter Cohort Study

ARTHRITIS & RHEUMATOLOGY
Vol. 66, No. 5, May 2014, pp 1101–1110

Cumulative incidence rates of spontaneous abortion



	MTX-exposed cohort		Disease-matched comparison	Non-autoimmune disease comparison
	pre-conception n=136	post-conception n=188	n=459	n=1107
Abortion	8.8%	20.7%	9.6%	7.1%
Major birth defects	3.5%	6.6%	3.6%	2.9%
Minor birth defects	4.4%	1.9%	5.6%	2.3%

Post-conception administration of MTX at dosages typically used in the treatment of rheumatic diseases was associated with an increased risk of major birth defects and spontaneous abortion.

Such evidence was not found among women in our pre-conception cohort.

Points to consider for use of anti rheumatic drugs in pregnancy

csDMARDs

tsDMARDs

Grade of recommendation

csDMARDs, tsDMARDs and anti-inflammatory drugs with **insufficient documentation** concerning use in pregnancy should be avoided until further evidence is available. This applies to **leflunomide and tofacitinib**.

Consensus on statements and expert opinion

Drug	Statement on compatibility of drug with pregnancy based on evidence	Percentage of agreement with statement	Expert opinion on use of drug in clinical practice*
Leflunomide	Current evidence is insufficientIn a planned pregnancy, a washout procedure should be completed before pregnancy Leflunomide should be avoided in pregnancy	100	
Tofacitinib	Current evidence is insufficientIn a planned pregnancy treatment with tofacitinib should be stopped 2 months before conception	100	

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I would recommend the drug in the same way as if the patient was not pregnant.
I would only recommend the drug if I feared at least moderate disease activity in its absence.
I would only recommend the drug if I feared at least severe disease activity in its absence.
I would never recommend the drug in pregnancy.

B Category II evidence from at least one controlled study without randomisation (2A) or from at least one type of quasi-experimental study (2B), or extrapolated recommendations from category I evidence.

D Category IV evidence from expert committee reports or opinions and/or clinical experience of respected authorities (4), or extrapolated recommendation from category II or III evidence

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Points to consider for use of anti rheumatic drugs in pregnancy

NSAIDs

Grade of recommendation

Non-steroidal anti-inflammatory drugs (**NSAIDs**) should be considered for use in pregnancy if needed to control active disease symptoms. NSAIDs should be restricted to the **first and second trimesters**. **B**

Selective COX II inhibitors have **insufficient documentation** concerning use in pregnancy and should be avoided until further evidence is available. **D**

Consensus on statements and expert opinion

Drug	Statement on compatibility of drug with pregnancy based on evidence	Percentage of agreement with statement	Expert opinion on use of drug in clinical practice*
Non-selective COX inhibitors (classical NSAIDs)	Current evidence indicates no increased rate of congenital malformationsNon-selective COX inhibitors can be continued during the first and second trimesters	92	
Selective COX II inhibitors	Current evidence is insufficientSelective COX II inhibitors should be avoided in pregnancy	100	

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I would recommend the drug in the same way as if the patient was not pregnant.
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I would only recommend the drug if I feared at least severe disease activity in its absence.
I would never recommend the drug in pregnancy.

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Points to consider for use of anti rheumatic drugs in pregnancy

Glucocorticoids

Grade of recommendation

Prednisone should be considered for use in pregnancy if needed to control active disease symptoms. **B**

In severe, refractory maternal disease during pregnancy methylprednisolone pulses should be considered. **D**

Consensus on statements and expert opinion

Drug	Statement on compatibility of drug with pregnancy based on evidence	Percentage of agreement with statement	Expert opinion on use of drug in clinical practice*
Prednisone	Current evidence indicates no increased rate of congenital malformations Prednisolone/prednisone can be continued at the lowest effective dose throughout pregnancy	100	
Intra-articular/ intramuscular glucocorticoids	Current evidence indicates no increased rate of congenital malformationsIntra-articular/ intramuscular glucocorticoids can be given, when required, throughout pregnancy	100	
Intravenous glucocorticoids	Current evidence indicates no increased rate of congenital malformations Intravenous glucocorticoids can be given, when required, throughout pregnancy	100	
Fluorinated glucocorticoids	Current evidence indicates that fluorinated glucocorticoids should be used with caution because they are less metabolised by the placentaThey should only be used to treat fetal problems	100	

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I would only recommend the drug if I feared at least severe disease activity in its absence.
I would never recommend the drug in pregnancy.

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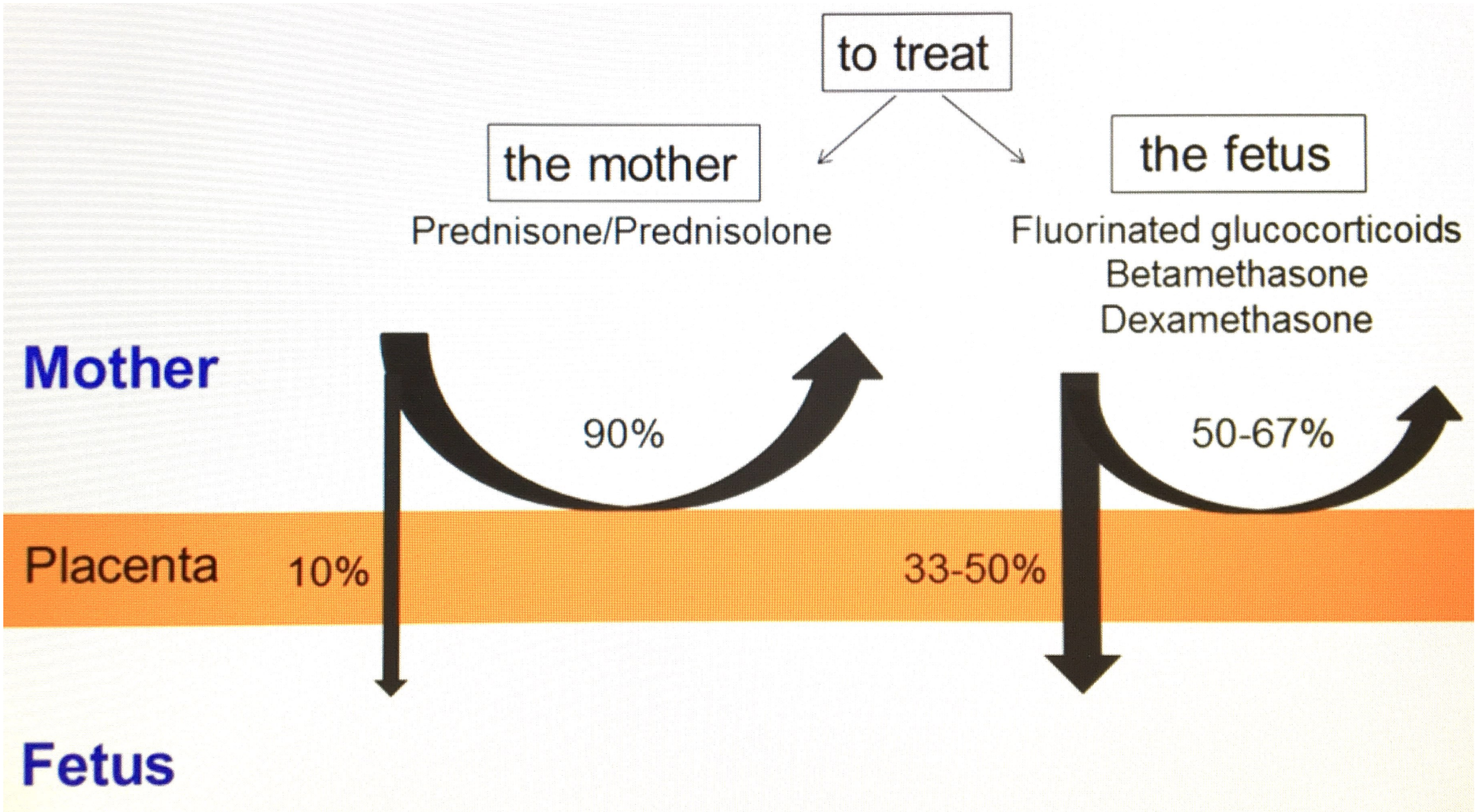
Glucocorticoids and placental transfer



Blandford AT AM J Obstet Gynecol 1977

Points to consider for use of anti rheumatic drugs in pregnancy

bDMARDs

Grade of recommendation

Among bDMARDs continuation of tumour necrosis factor (TNF) inhibitors during the first part of pregnancy should be considered. **Etanercept** and **certolizumab** may be considered for use throughout pregnancy due to low rate of transplacental passage.

Consensus on statements and expert opinion

Drug	Statement on compatibility of drug with pregnancy based on evidence	Percentage of agreement with statement	Expert opinion on use of drug in clinical practice (%)*
Etanercept	Current evidence indicates no increased rate of congenital malformations; etanercept can be continued up to gestational week 30–32; if indicated, it can be used throughout pregnancy	100	
Certolizumab	Current evidence indicates no increased rate of congenital malformations; certolizumab can be continued throughout pregnancy	100	

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I would recommend the drug in the same way as if the patient was not pregnant.
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I would never recommend the drug in pregnancy.

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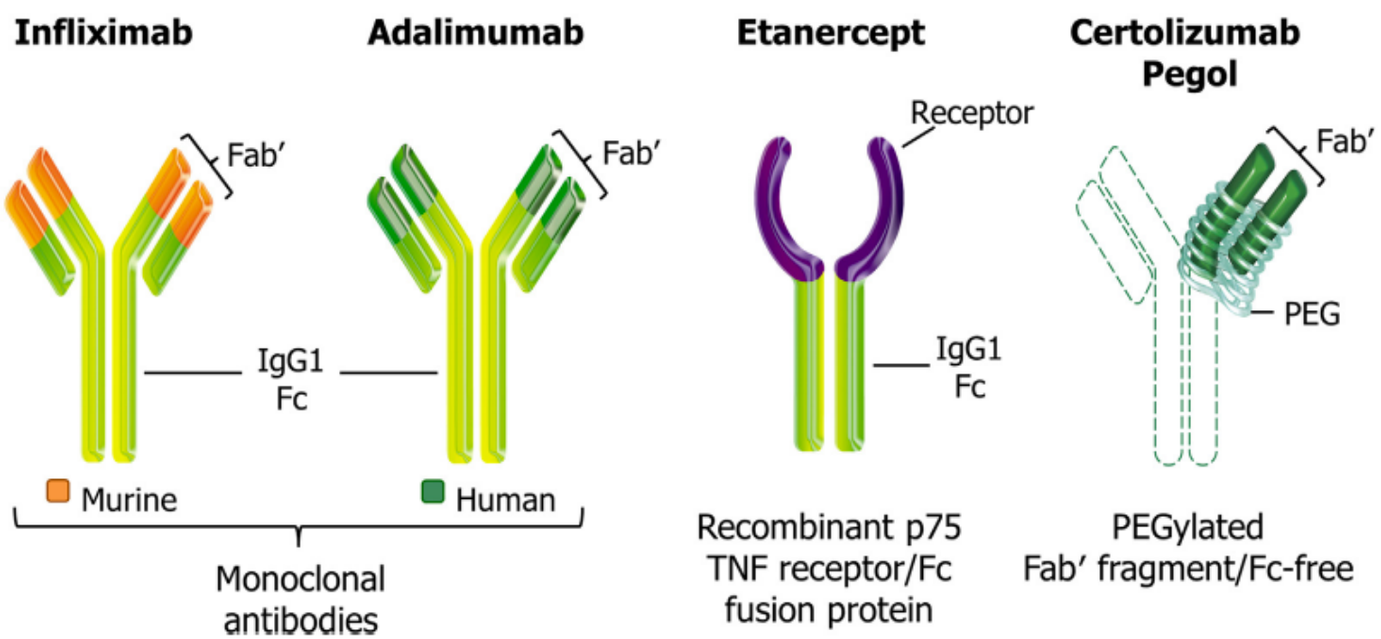
Certolizumab pegol does not bind the neonatal Fc receptor (FcRn): Consequences for FcRn-mediated *in vitro* transcytosis and *ex vivo* human placental transfer

Journal of Reproductive Immunology 116 (2016) 7–12



The active transfer of these antibodies across the placenta by binding of the Fc-region to the neonatal Fc receptor (FcRn) may result in adverse fetal or neonatal effects.

In contrast to other anti-TNFs, certolizumab pegol lacks an Fc-region.

- The plasma half-life of CZP is prolonged by the presence of a PEG moiety.
- The impact on the fetus is lessened by the unique structure of CZP and resultant extremely low placental transfer
- CZP was not detected in breast milk.
- Given its reported minimal placental transfer, it has been recommended that CZP may be continued throughout pregnancy.

Points to consider for use of anti rheumatic drugs in pregnancy

bDMARDs

bDMARDs **rituximab, infliximab, adalimumab, golimumab, anakinra, tocilizumab, abatacept, and ustekinumab** have limited documentation on safe use in pregnancy and should be **replaced before conception** by other medication. They should be used during pregnancy only when no other pregnancy-compatible drug can effectively control maternal disease.

Grade of recommendation

Consensus on statements and expert opinion

Drug	Statement on compatibility of drug with pregnancy based on evidence	Percentage of agreement with statement	Expert opinion on use of drug in clinical practice (%)*
Infliximab	Current evidence indicates no increased rate of congenital malformations; infliximab can be continued up to gestational week 20; if indicated, it can be used throughout pregnancy	100	
Adalimumab	Current evidence indicates no increased rate of congenital malformations; adalimumab can be continued up to gestational week 20; if indicated, it can be used throughout pregnancy	100	
Golimumab	Current evidence does not indicate an increased rate of congenital malformations; because of limited evidence, alternative medications should be considered for treatment throughout pregnancy	100	
Rituximab	Current evidence indicates no increased rate of congenital malformations; in exceptional cases it can be used early in gestation; with use at later stages of pregnancy clinicians should be aware of the risk of B cell depletion and other cytopenias in the neonate	100	
Anakinra	Current evidence does not indicate an increased rate of congenital malformations; anakinra can be used before and during pregnancy when there are no other well studied options available for treatment	100	
Ustekinumab	Current evidence does not indicate an increased rate of congenital malformations; because of limited evidence, alternative medications should be considered for treatment throughout pregnancy	100	
Tocilizumab	No statement can be made in regard to safety during pregnancy due to scarce documentation; treatment with tocilizumab is therefore best avoided	100	
Abatacept	No statement can be made in regard to safety during pregnancy due to scarce documentation; treatment with abatacept is therefore best avoided	94	

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I would only recommend the drug if I feared at least severe disease activity in its absence.
I would never recommend the drug in pregnancy.

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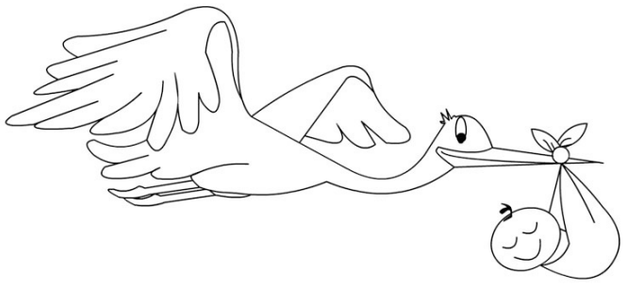


☑ Pregnancy planning

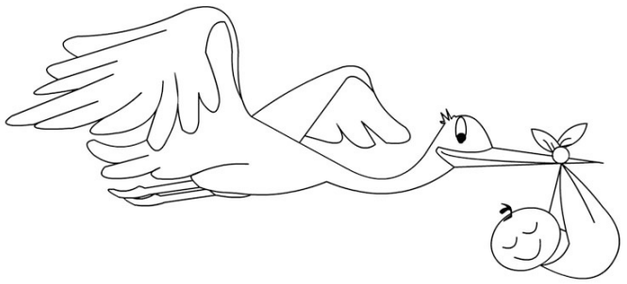
Management of RA during pregnancy and lactation requires weighing risks of withholding treatment from the mother against any risk to the fetus/child via exposure to drugs during pregnancy or breast feeding

☑ Antirheumatic drugs in pregnancy

HCQ,CQ, SSZ, AZA, CsA, NSAIDs (I, II trimester)
certolizumab, etanercept (I trimester),
prednisone, methylprednisolone pulses

leflunomide, tofacitinib, selective COX II inhib, RTX, anakinra, tocilizumab, abatacept, ustekinumab, other antiTNF

MTX
MMF
CTX



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certolizumab, etanercept (I trimester),
prednisone, methylprednisolone pulses

leflunomide, tofacitinib, selective COX II inhib, RTX, anakinra, tocilizumab, abatacept, ustekinumab, other antiTNF

MTX
MMF
CTX

☐ Antirheumatic drugs during lactation

Points to consider for use of anti rheumatic drugs during lactation

csDMARDs

Grade of recommendation

csDMARDs **compatible** with breast feeding should be considered for continuation during lactation provided the child does not have conditions that contraindicate it. This applies to **hydroxychloroquine, chloroquine, sulfasalazine, azathioprine, ciclosporin**.

Consensus on statements and expert opinion

Drug	Statement on compatibility of drug with breast feeding based on evidence	Percentage of agreement with statement	Expert opinion on use of drug during breast feeding†
Hydroxychloroquine	Hydroxychloroquine is compatible with breast feeding	100	
Chloroquine	Chloroquine is compatible with breast feeding	88	
Sulfasalazine	Sulfasalazine is compatible with breast feeding in the healthy, full-term infant	94	
Azathioprine	Azathioprine is compatible with breast feeding	94	
Ciclosporin	Ciclosporin is compatible with breast feeding	100	

*As an expert in the field.
I would recommend the drug in the same way as if the patient was not pregnant.
I would only recommend the drug if I feared at least moderate disease activity in its absence.
I would only recommend the drug if I feared at least severe disease activity in its absence.
I would never recommend the drug in pregnancy.

D Category IV evidence from expert committee reports or opinions and/or clinical experience of respected authorities (4), or extrapolated recommendation from category II or III evidence

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Points to consider for use of anti rheumatic drugs during lactation

csDMARDs

tsDMARDs

Grade of recommendation

csDMARDs and tsDMARDs with no or limited data on breast feeding **should be avoided** in lactating women. This applies to **methotrexate, mycophenolate mofetil, cyclophosphamide, leflunomide and tofacitinib**.

Consensus on statements and expert opinion

Drug	Statement on compatibility of drug with breast feeding based on evidence	Percentage of agreement with statement	Expert opinion on use of drug during breast feeding†
Methotrexate	Only small amounts of methotrexate appear in breast milk, but data are limited, therefore methotrexate should be avoided in breast feeding	100	
Cyclophosphamide	There are limited data regarding cyclophosphamide in breast milk, therefore cyclophosphamide should be avoided in breast feeding	94	
Tofacitinib	No data exist regarding tofacitinib in breast milk, therefore tofacitinib should be avoided in breast feeding	100	
Mycophenolate mofetil (MMF)	No data exist regarding MMF in breast milk, therefore MMF should be avoided in breast feeding	100	
Leflunomide	No data exist regarding leflunomide in breast milk, therefore leflunomide should be avoided in breast feeding	100	

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I would recommend the drug in the same way as if the patient was not pregnant.
I would only recommend the drug if I feared at least moderate disease activity in its absence.
I would only recommend the drug if I feared at least severe disease activity in its absence.
I would never recommend the drug in pregnancy.

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Götestam Skorpen C, *et al. Ann Rheum Dis* 2016;**0**:1–16.

Points to consider for use of anti rheumatic drugs during lactation

NSAIDs

Grade of recommendation

Anti-inflammatory drugs **compatible** with breast feeding should be considered for continuation during lactation provided the child does not have conditions that contraindicate it. This applies to **non-selective COX inhibitors and celecoxib**.

And anti-inflammatory drugs with no or limited data on breast feeding should be **avoided** in lactating women. This applies to **cyclooxygenase II inhibitors other than celecoxib**.

Consensus on statements and expert opinion

Drug	Statement on compatibility of drug with breast feeding based on evidence	Percentage of agreement with statement	Expert opinion on use of drug during breast feeding†
Non-selective COX inhibitors (classical NSAIDs)	Non-selective COX inhibitors are compatible with breast feeding	88	
Selective COX II inhibitors	Among COX II inhibitors only celecoxib has been sufficiently studied; celecoxib is compatible with breast feeding, other COX II inhibitors should be avoided during lactation	94	

*As an expert in the field.
I would recommend the drug in the same way as if the patient was not pregnant.
I would only recommend the drug if I feared at least moderate disease activity in its absence.
I would only recommend the drug if I feared at least severe disease activity in its absence.
I would never recommend the drug in pregnancy.

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Points to consider for use of anti rheumatic drugs during lactation

Glucocorticoids

Grade of recommendation

Anti-inflammatory drugs **compatible** with breast feeding should be considered for continuation during lactation provided the child does not have conditions that contraindicate it. This applies to **prednisone**.

Consensus on statements and expert opinion

Drug	Statement on compatibility of drug with breast feeding based on evidence	Percentage of agreement with statement	Expert opinion on use of drug during breast feeding†
Prednisone	Glucocorticoids are compatible with breast feeding	100	

*As an expert in the field.
I would recommend the drug in the same way as if the patient was not pregnant.
I would only recommend the drug if I feared at least moderate disease activity in its absence.
I would only recommend the drug if I feared at least severe disease activity in its absence.
I would never recommend the drug in pregnancy.

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Götestam Skorpen C, *et al. Ann Rheum Dis* 2016;**0**:1–16.

Points to consider for use of anti rheumatic drugs during lactation

bDMARDs

Grade of recommendation

Low transfer to breast milk has been shown for **infliximab, adalimumab, etanercept and certolizumab**. Continuation of TNF inhibitors should be considered **compatible** with breast feeding.

Consensus on statements and expert opinion

Drug	Statement on compatibility of drug with breast feeding based on evidence	Percentage of agreement with statement	Expert opinion on breast feeding and medication (%)†
Infliximab	Infliximab is compatible with breast feeding	100	
Adalimumab	Adalimumab is compatible with breast feeding	100	
Etanercept	Etanercept is compatible with breast feeding	100	
Certolizumab	Certolizumab is compatible with breast feeding	94	

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I would recommend the drug in the same way as if the patient was not pregnant.
I would only recommend the drug if I feared at least moderate disease activity in its absence.
I would only recommend the drug if I feared at least severe disease activity in its absence.
I would never recommend the drug in pregnancy.

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Points to consider for use of anti rheumatic drugs during lactation

bDMARDs

bDMARDs with no data on breast feeding such as **rituximab, anakinra, ustekinumab, tocilizumab and abatacept** **should be avoided** during lactation if other therapy is available to control the disease. Based on pharmacological properties of bDMARDs, lactation should not be discouraged when using these agents, if no other options are available.

Grade of recommendation

*As an expert in the field.
I would recommend the drug in the same way as if the patient was not pregnant.
I would only recommend the drug if I feared at least moderate disease activity in its absence.
I would only recommend the drug if I feared at least severe disease activity in its absence.
I would never recommend the drug in pregnancy.

Consensus on statements and expert opinion

Drug	Statement on compatibility of drug with breast feeding based on evidence	Percentage of agreement with statement	Expert opinion on breast feeding and medication (%)†
Rituximab	No data exist regarding rituximab in breast milk, therefore rituximab should be avoided in breast feeding	80	
Anakinra	No data exist regarding anakinra in breast milk, therefore anakinra should be avoided in breast feeding	88	
Ustekinumab	No data exist regarding ustekinumab in breast milk, therefore ustekinumab should be avoided in breast feeding	75	
Tocilizumab	No data exist regarding tocilizumab in breast milk, therefore tocilizumab should be avoided in breast feeding	69	
Abatacept	No data exist regarding abatacept in breast milk, therefore abatacept should be avoided in breast feeding	75	

D Category IV evidence from expert committee reports or opinions and/or clinical experience of respected authorities (4), or extrapolated recommendation from category II or III evidence

Götestam Skorpen C, *et al. Ann Rheum Dis* 2016;**0**:1–16.

Pregnancy planning

Management of RA during pregnancy and lactation requires weighing risks of withholding treatment from the mother against any risk to the fetus/child via exposure to drugs during pregnancy or breast feeding

Antirheumatic drugs in pregnancy

HCQ,CQ, SSZ, AZA, CsA, NSAIDs (I, II trimester) certolizumab, etanercept (I trimester), prednisone, methylprednisolone pulses

leflunomide, tofacitinib, selective COX II inhib, RTX, anakinra, tocilizumab, abatacept, ustekinumab, other antiTNF

MTX
MMF
CTX

Antirheumatic drugs during lactation

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RTX, anakinra, Tocilizumab, abatacept, ustekinumab

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MTX, MMF, CTX, leflunomide, tofacitinib, selective COX II inhib

☐ Unplanned pregnancy

Unplanned Pregnancies

- Some patients opt for immediate termination whereas others contemplate continuation of the pregnancy.
- Confirmation of pregnancy by a gynaecologist and determination of exact exposure dates for individual risk assessment and counselling are mandatory.
- A detailed ultrasound examination of the fetus should be offered to all patients who have an unintended pregnancy while taking a teratogenic drug. Macroscopic anomalies can be assessed by experienced fetal medicine specialists at the end of the first trimester and scans should be repeated at later stages of the second trimester.
- Other prenatal tests like amniocentesis or chorionic villous biopsy are usually not indicated after maternal drug exposure, but might be considered in patients with high risk of chromosomal problems or anomalies at ultrasound examination.

Götestam Skorpen C, *et al*. *Ann Rheum Dis* 2016;**0**:1–16.

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RTX, anakinra, Tocilizumab, abatacept, ustekinumab

MTX, MMF, CTX, leflunomide, tofacitinib, selective COX II inhib

Unplanned pregnancy

An ultrasound examination should be done to all patients who have an unintended pregnancy while taking a teratogenic drug. Amniocentesis or chorionic villous biopsy are usually not indicated after maternal drug exposure, but might be considered in patients with high risk of chromosomal problems or anomalies at ultrasound examination.

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☐ Paternal exposure

Paternal exposure

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BRIEF REPORT

No Excess Risks in Offspring With Paternal Preconception Exposure to Disease-Modifying Antirheumatic Drugs

Marianne Wallenius,[1] Elisabeth Lie,[2] Anne K. Daltveit,[3] Kjell Å. Salvesen,[4] Johan F. Skomsvoll,[5] Synøve Kalstad,[6] Åse S. Lexberg,[7] Knut Mikkelsen,[8] Tore K. Kvien,[2] and Monika Østensen[5]

196 Scand J Rheumatol 2012;41:196–201

Outcomes after anti-rheumatic drug use before and during pregnancy: a cohort study among 150 000 pregnant women and expectant fathers

KK Viktil[1,2], A Engeland[3,4], K Furu[3,5]

[1]Diakonhjemmet Hospital Pharmacy, Oslo, [2]School of Pharmacy, University of Oslo, [3]Department of Pharmacoepidemiology, Norwegian Institute of Public Health, Oslo, [4]Department of Public Health and Primary Health Care, University of Bergen, and [5]Department of Pharmacy, University of Tromsø, Norway

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Published online 8 June 2009 in Wiley InterScience (www.interscience.wiley.com) **DOI**: 10.1002/pds.1775

ORIGINAL REPORT

Use of antirheumatic drugs in mothers and fathers before and during pregnancy—a population-based cohort study†

Kirsten K Viktil PhD, MSc Pharm[1*,‡], Anders Engeland PhD, MSc[2§] and Kari Furu PhD, MSc[3¶]

[1]*Diakonhjemmet Hospital Pharmacy, Oslo and Department of Pharmacotherapeutics, Diakonhjemmet Hospital Pharmacy, Faculty of Medicine, University of Oslo, Oslo, Norway*
[2]*Department of Pharmacoepidemiology, Norwegian Institute of Public Health, Oslo and Department of Public Health and Primary Health Care, University of Bergen, Bergen, Norway*
[3]*Department of Pharmacoepidemiology, Norwegian Institute of Public Health, Oslo, Norway*

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Original article

No evidence for an increased risk of adverse pregnancy outcome after paternal low-dose methotrexate: an observational cohort study

Corinna Weber-Schoendorfer[1], Maria Hoeltzenbein[1], Evelin Wacker[1], Reinhard Meister[2] and Christof Schaefer[1]

Preconception paternal exposure to DMARDs was not associated with an increase in adverse pregnancy outcomes.
No increased risk of congenital malformations was observed.

Pregnancy planning

Management of RA during pregnancy and lactation requires weighing risks of withholding treatment from the mother against any risk to the fetus/child via exposure to drugs during pregnancy or breast feeding

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Unplanned pregnancy

An ultrasound examination should be done to all patients who have an unintended pregnancy while taking a teratogenic drug. Amniocentesis or chorionic villous biopsy are usually not indicated after maternal drug exposure, but might be considered in patients with high risk of chromosomal problems or anomalies at ultrasound examination.

Paternal exposure

Preconception paternal exposure to DMARDs is not associated with an increase in adverse pregnancy outcomes. No increased risk of congenital malformations was observed.

☑ Pregnancy planning

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☐ Follow up of children

FOLLOW-UP OF CHILDREN

- The available data for several biologics and immunosuppressives show **no adverse effects** on physical or neurocognitive development **nor impaired immunocompetence** in children during the 1st year of life.
- **Biologics** when administered **after gestational week 30**, **might increase the risk of postnatal infection**.
- Children exposed to biologics only **before week 22 can receive vaccinations** according to standard protocols including live vaccines.
- **Children exposed at the late second and during the third trimester** can follow vaccination programmes, but should **not receive live vaccines in the first 6 months of life**.

Götestam Skorpen C, *et al*. *Ann Rheum Dis* 2016;**0**:1–16.

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Preconception paternal exposure to DMARDs was not associated with an increase in adverse pregnancy outcomes. No increased risk of congenital malformations was observed.

Follow up of children

Biologics when administered after gestational week 30, might increase the risk of postnatal infection.

- Effective drug treatment of active RA is possible with reasonable safety
- Restriction in use apply for few proven teratogenic drugs and the large proportion of medications for which insufficient safety data are available
- Among biologics TNF inhibitors are best studied and appear not to increase the rate of congenital malformations
- In the most recent guidance (EULAR points to consider and BSR) certolizumab is the only anti-TNF that can be continued throughout pregnancy