

# Effect of folic acid supplementation and allopurinol on blood vessel health in patients with rheumatoid arthritis

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<b>Registration date</b> 09/05/2008	<b>Overall study status</b> Stopped	<input type="checkbox"/> Protocol
<b>Last Edited</b> 21/06/2017	<b>Condition category</b> Musculoskeletal Diseases	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

Not provided at time of registration

## Contact information

### Type(s)

Scientific

### Contact name

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### Contact details

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## Additional identifiers

### Protocol serial number

MTXa54 v1 04/04/05

## Study information

**Scientific Title**

Effect of folic acid supplementation and allopurinol on endothelial function in patients with rheumatoid arthritis treated with methotrexate

**Study objectives**

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disorder characterized by a symmetrical erosive polyarthritis with inflammatory multisystemic involvement. Most patients exhibit a chronic fluctuating course of disease that, if left untreated, results in progressive joint destruction, deformity, and disability. The patient with RA has their life span shortened by 15-20% with up to 40% of excess deaths being due to cardiovascular disease.

**Study aim:**

To evaluate whether endothelial function and other surrogate markers of cardiovascular disease can be improved by the addition of extra folic Acid (above the dose conventionally given) and allopurinol (which attenuates oxidative stress) in patients with RA taking methotrexate.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Tayside Committee on Medical Research Ethics, 26/05/2005, ref: 05/S1401/55

**Study design**

Single-centre randomised double-blind placebo-controlled trial

**Primary study design**

Interventional

**Study type(s)**

Treatment

**Health condition(s) or problem(s) studied**

Rheumatoid arthritis

**Interventions**

The participants will be randomised to the following:

Control group: 5 mg of folic acid (oral) once a week as per methotrexate protocol

"Active" group: 5 mg of folic acid (oral) 7 days a week (extra folic acid)

At 4 months, both groups will be randomised again to receive either allopurinol (oral) 300 mg a day or placebo in addition to their folate/control medication for 8 weeks.

**Intervention Type**

Drug

**Phase**

Not Applicable

**Drug/device/biological/vaccine name(s)**

Folic acid, allopurinol and methotrexate

### **Primary outcome(s)**

Endothelial function measured by the following at baseline, 4 and 6 months:

1. Laser Doppler flowmetry after iontophoretic delivery of acetylcholine and sodium nitroprusside (microvascular)
2. Brachial artery flow mediated dilatation (macrovascular)

### **Key secondary outcome(s)**

The following were assessed at baseline, 4 and 6 months:

1. Endothelial function measured by blood testing of vascular function and damage (E selectin, thrombomodulin)
2. Arterial stiffness measured by applanation tonometry
3. Oxidative stress (Isoprostane levels)
4. Serum homocysteine, folic acid and uric acid levels
5. RA disease activity (28-item Disease Activity Score [DAS28], Health Assessment Questionnaire [HAQ], the 36-item short form health survey [SF-36])

### **Completion date**

14/03/2008

### **Reason abandoned (if study stopped)**

Lack of funding/sponsorship

## **Eligibility**

### **Key inclusion criteria**

1. Both males and females, 18 years old or over
2. Fulfil the 1987 American College of Rheumatology (ACR) classification criteria for RA
3. On methotrexate for at least 6 months

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

18 years

### **Sex**

All

### **Key exclusion criteria**

1. Previous cardiovascular or cerebrovascular events in the last 3 years
2. Undergoing treatment for a cardiovascular risk factor except:
  - 2.1. Patients with hypertension on stable medication for the last 3 months

- 2.2. Patients with hypercholesterolemia on stable medication for the last 3 months  
3. Contraindications to allopurinol (moderate to severe renal impairment, liver impairment, concomitant treatment with azathioprine, known allergy to allopurinol)

**Date of first enrolment**

21/08/2006

**Date of final enrolment**

14/03/2008

## **Locations**

**Countries of recruitment**

United Kingdom

Scotland

**Study participating centre**

**Vascular and Inflammatory Diseases Research Unit**

Dundee

United Kingdom

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## **Sponsor information**

**Organisation**

University of Dundee (UK)

**ROR**

<https://ror.org/03h2bxq36>

## **Funder(s)**

**Funder type**

Charity

**Funder Name**

Tenovus Scotland (ref: T05/31) (UK)

**Funder Name**

Anonymous Trust, University of Dundee (UK)

## **Results and Publications**

**Individual participant data (IPD) sharing plan**

**IPD sharing plan summary**

Not provided at time of registration