

# **EFFECT OF ISCHAEMIA-REPERFUSION ON RABBIT KIDNEY AND HUMAN BRAIN**

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## **Jagdish Gondalia**

- I. Enhanced post-ischaeamic recovery in rabbit kidney after pretreatment with an indeno-indole compound and ascorbate monitored in vivo by  $^{31}\text{P}$  magnetic resonance spectroscopy.  
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- II. Effects of pretreatment with a xanthine oxidase inhibitor on free radical levels during carotid endarterectomy.  
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- III. Effect of pretreatment with N-acetylcysteine on free radical levels during carotid endarterectomy.  
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- IV. Relationships between free radical levels during carotid endarterectomy and markers of arteriosclerotic disease.  
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**Fakultetsopponent: Professor Börje Ljungberg  
Urologiska kliniken, Norrlands Universitetssjukhus, Umeå**

## Abstract

### Effect of Ischaemia-Reperfusion on Rabbit Kidney and Human Brain

Jagdish Gondalia, MD, Institute of Clinical Sciences, Department of Urology  
The Sahlgrenska Academy at Göteborg University, Sahlgrenska University Hospital  
SE-413 45 Göteborg, Sweden

Free radicals are produced in various organs at ischaemia-reperfusion. The final stage in radical damage is lipid peroxidation. We have demonstrated previously that a lipid-soluble antioxidant improves restoration of bioenergetics in rabbit kidneys after ischaemia, as reflected in  $^{31}\text{P}$  spectrometry. Radical production in the brain during surgery for carotid artery stenosis can be measured using an *ex vivo* spin trap method.

**Aims of the present study:** 1. To examine whether pretreatment with a combination of a lipid-soluble and a water-soluble antioxidant causes improved restoration of bioenergetics in rabbit kidneys after ischaemia compared to single treatment with a lipid soluble antioxidant. 2. To examine whether pretreatment with allopurinol or acetylcysteine influences radical production in conjunction with surgery for carotid artery stenosis. 3. To study the relationship between various markers for arteriosclerosis and the production of free radicals in conjunction with surgery for carotid artery stenosis.

**Methods:** New Zealand white rabbits were used for the NMR experiments. Volume-selective  $^{31}\text{P}$  spectrometry was used to determine changes in bioenergetics during and after ischaemia following various pretreatments. An *ex vivo* spin trap method was used to measure radical production in the brain during carotid endarterectomy in control patients as well as patients pretreated with allopurinol or acetylcysteine. ICAM-1, MCP-9, MMP-1 and oxLDL serum levels were determined in the control patients.

**Results:** Pretreatment with a combination of a lipid-soluble and a water-soluble antioxidant resulted in improved restoration in cell bioenergetics after ischaemia compared to single treatment with a lipid-soluble antioxidant. Production of radicals can be measured reproducibly using the *ex vivo* spin trap method. Pretreatment with allopurinol eliminated the strong correlation between e.g. degree of stenosis and leucocyte counts and radical production, which might indicate a beneficial effect of pretreatment with a xanthine oxidase inhibitor. Pretreatment with acetylcysteine on the other hand appeared to increase radical production. High levels of MMP-1 and low levels of ICAM-1 were associated with high radical production.

**Conclusion:** A combination of a lipid-soluble and a water-soluble antioxidant is most effective in improving cell bioenergetics after ischaemia in rabbit kidneys. Allopurinol appears to have a beneficial effect in conjunction with carotid endarterectomy while acetylcysteine appears to increase radical production. MMP-1 is associated with increased radical production.

**Keywords:** Free radicals, ischaemia-reperfusion, cell bioenergetics, NMR, ESR, carotid artery stenosis, endarterectomy, allopurinol, acetylcysteine, MMP-1, ICAM-1, MCP-9, oxLDL.

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