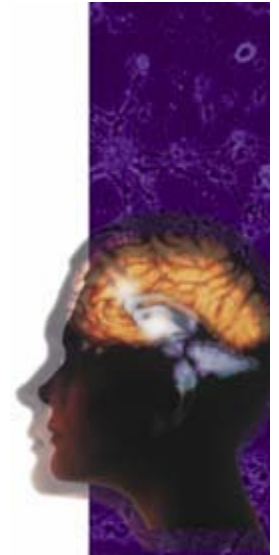


# N-ACETYLCYSTEINE (NAC)

This article was prepared by Malcolm R Hooper - HyperMED Australia

- N-acetylcysteine is an amino acid which is widely used as an antioxidant both directly as a glutathione substitute and indirectly as a precursor for glutathione (neurotransmitter).
- Supplementation of hyperbaric oxygen therapy with N-acetylcysteine appears to increase fibroblast proliferation promoting neuro-musculoskeletal function and repair.
- N-acetylcysteine causes vasodilatation; NAC may be of benefit in acute myocardial infarction and other chronic ischemic disorders.
- N-acetylcysteine neuro-protective effect preventing trauma-induced oxidative brain tissue damage.
- N-acetylcysteine promotes and protects Blood Brain Barrier (BBB) function.
- N-acetylcysteine reduces chronic BBB inflammation and swelling causing hypoxia.
- N-acetylcysteine results in a reduction body weights, and a marked reduction in visceral fat tissues (adipogenesis). N-acetylcysteine may be useful as an anti-obesity drug or supplement.
- N-acetylcysteine enhances T cell function in HIV infected patients and other chronic immunosuppressive disorders.
- N-acetylcysteine high-dose oral has the potential to counter the intertwined redox and inflammatory imbalances associated with Cystic Fibrosis and other obstructive airways disorders and chronic respiratory infections.
- N-acetylcysteine, is widely used as an antioxidant, but also protects pancreatic beta cells in type 1 diabetes.
- Methylsulphonylmethane is a strong antioxidant of the methionine cycle; combined with N-acetyl cysteine providing strong neuroprotection promoting recovery and stabilization.



## [Blood-brain barrier dysfunction and recovery]

Blood-Brain Barrier Research Group, Division of Pharmacology, Leiden/Amsterdam Center for Drug Research, University of Leiden, Gorlaeus Laboratories, Leiden, The Netherlands. [J Neural Transm.](#) 2006 Apr; 113(4):455-62.

In this paper we discuss the importance of the blood-brain barrier (BBB) as an interface between blood and brain. Many (brain) diseases change the functionality and integrity of the BBB. Mostly this results in increased BBB permeability. Therefore we have studied de various signal transduction routes that are influenced by inflammatory stimuli. The radical scavenger **N-acetylcysteine was able to protect the BBB against inflammatory stimuli**. Similar results were found following application of glucocorticoids. In addition, it was observed that glucocorticoids and interferon-alpha,beta increased the tightness of the in vitro BBB and when given together a potentiating effect was seen.

## [Neuroprotective Effects of N-acetylcysteine on Experimental Closed Head Trauma in Rats]

Faculty of Medicine, Department of Neurosurgery, Trakya University, Edirne, Turkey. *Neurochem Res.* 2006 May 9.

**N-acetylcysteine (NAC) is a precursor of glutathione, a potent antioxidant, and a free radical scavenger. The beneficial effect of NAC on nervous system ischemia and ischemia/reperfusion models** has been well documented. However, the effect of NAC on nervous system trauma remains less understood. Therefore, we aimed to investigate the therapeutic efficacy of NAC with an experimental closed head trauma model in rats. Thirty-six adult male Sprague-Dawley rats were randomly divided into three groups of 12 rats each: Group I (control), Group II (trauma-alone), and Group III (trauma+NAC treatment). In Groups II and III, a cranial impact was delivered to the skull from a height of 7 cm at a point just in front of the coronal suture and over the right hemisphere. Rats were sacrificed at 2 h (Subgroups I-A, II-A, and III-A) and 12 h (Subgroups I-B, II-B, and III-B) after the onset of injury. Brain tissues were removed for biochemical and histopathological investigation. The closed head trauma significantly increased tissue malondialdehyde (MDA) levels ( $P<0.05$ ), and significantly decreased tissue superoxide dismutase (SOD) and glutathione peroxidase (GPx) activities ( $P<0.05$ ), but not tissue catalase (CAT) activity, when compared with controls. The administration of a single dose of NAC (150 mg/kg) 15 min after the trauma has shown **protective effect via decreasing significantly the elevated MDA levels ( $P<0.05$ ) and also significantly ( $P<0.05$ ) increasing the reduced antioxidant enzyme (SOD and GPx) activities**, except CAT activity. In the trauma-alone group, the neurons became extensively dark and degenerated into picnotic nuclei. **The morphology of neurons in the NAC treatment group was well protected.** The number of neurons in the trauma-alone group was significantly less than that of both the control and trauma+NAC treatment groups. In conclusion, the **NAC treatment might be beneficial in preventing trauma-induced oxidative brain tissue damage, thus showing potential for clinical implications.**

## [Combined effect of hyperbaric oxygen and N-acetylcysteine on fibroblast proliferation]

Wound Healing and Tissue Engineering Laboratory, Department of Otolaryngology-Head and Neck Surgery, Stanford University School of Medicine, Stanford, Calif., USA. [Arch Otolaryngol Head Neck Surg.](#) 2005 Sep; 131(9):809-14

**OBJECTIVE:** To examine the **combined effect of hyperbaric oxygen and N-acetylcysteine, a well-studied antioxidant, on fibroblast proliferation and production of 3 specific growth factors: basic fibroblast growth factor, vascular endothelial growth factor, and transforming growth factor beta1.** **DESIGN:** In vitro study. **SUBJECTS:** None. **INTERVENTIONS:** Human dermal fibroblasts were propagated in serum-free medium and subjected to daily 90-minute 2-atm hyperbaric oxygen treatments with varying concentrations of N-acetylcysteine for 7 consecutive days. Cell proliferation and growth factor assays were performed on days 0, 1, 3, 5, and 7. **RESULTS:** Population doubling time decreased significantly with 40 micromol/L of N-acetylcysteine supplementation of 2-atm hyperbaric oxygen treatment. Higher levels of N-acetylcysteine increased population doubling time. **CONCLUSIONS:** **Supplementation of hyperbaric oxygen therapy with 40 micromol/L of N-acetylcysteine appears to increase fibroblast proliferation without producing an unfavorable growth factor profile for normal healing. This**

suggests that this level of N-acetylcysteine may foster an ideal redox environment for fibroblast proliferation in a hyperbaric oxygen environment.

**[Dietary supplementation with 3-deaza adenosine, N-acetyl cysteine, and S-adenosyl methionine provide neuroprotection against multiple consequences of vitamin deficiency and oxidative challenge: relevance to age-related Neurodegeneration]**

Center for Cellular Neurobiology and Neurodegeneration Research, Department of Biological Sciences, University of Massachusetts Lowell, Lowell, MA 01854, USA. Neuromolecular Med. 2004; 6(2-3):93-103.

Folate deprivation induces neurotoxicity that is potentiated by additional nutritional and genetic deficiencies including vitamin E and apolipoprotein E deficiency. **These deficiencies collectively induce oxidative damage, cognitive impairment, and compensatory alteration in glutathione generation.** Treatment with agents that regulate distinct portions of the methionine cycle, including the S-adenosyl homocysteine hydrolase inhibitor, 3-deaza adenosine, the methyl donor S-adenosyl methionine, and the **antioxidant N-acetyl cysteine, provide neuroprotection against various aspects of neurotoxicity** in normal and apolipoprotein E-deficient mice and in cultured neuronal cells deprived of dietary folate and vitamin E and subjected to iron overload. Here it is demonstrated that simultaneous treatment with these agents provide superior neuroprotection by alleviating individual and overlapping neurotoxic consequences. These findings support combinatorial treatments with agents that compensate for differential insults in age-related neurodegenerative disorders.

[Methylsulphonylmethane is a strong antioxidant of the methionine cycle: combined with N-acetyl cysteine providing strong neuroprotection promoting recovery and stabilization]

**[Association of anti-obesity activity of N-acetylcysteine with metallothionein-II down-regulation]**

Department of Biochemistry and Molecular Biology, College of Medicine, Yeungnam University, Daegu 705-717, Korea. Exp Mol Med. 2006 Apr 30; 38(2): 162-72.

**People with upper body or visceral obesity have a much higher risk of morbidity and mortality from obesity-related metabolic disorders than those with lower body obesity.** In an attempt to develop therapeutic strategies targeting visceral obesity, depot- specific differences in the expression of genes in omental and subcutaneous adipose tissues were investigated by DNA array technology, and their roles in adipocyte differentiation were further examined. We found that levels of metallothionein-II (MT-II) mRNA and protein expression were higher in omental than in subcutaneous adipose tissues. The study demonstrates that MT-II may play an important role in adipocyte differentiation of 3T3L1 preadipocytes, and that N-acetylcysteine (NAC) inhibits the adipocyte differentiation of 3T3L1 cells by repressing MT-II in a time- and dose-dependent manner. Furthermore, the intraperitoneal administration of NAC to rats and mice resulted in a reduction of body weights, and a marked reduction in visceral fat tissues. These results suggest that MT-II plays important roles in adipogenesis, and that NAC may be useful as an anti-obesity drug or supplement.

**[The use of N-acetylcysteine in intensive care]**

Department of Anaesthesia, Royal Infirmary of Edinburgh, Edinburgh, Scotland mkat40@hotmail.com. Crit Care Resusc. 2002 Mar; 4(1):21-7.

OBJECTIVE: To review the actions and clinical use of serum N-acetylcysteine in the critically ill patient. DATA SOURCES: A review of articles published on the mechanisms of action and clinical use of N-acetylcysteine. SUMMARY OF REVIEW: **N-acetylcysteine (NAC) is an amino acid with a MW of 163.2. It acts as an antioxidant, both directly as a glutathione substitute and indirectly as a precursor for glutathione. It also causes vasodilation** by increasing cyclic guanosine monophosphate levels, inhibits platelet aggregation, acts as a sulphhydryl donor to regenerate endothelial-derived relaxing factor and reduces IL-8 and TNF- $\alpha$  production. While there is evidence for its effectiveness as an antidote to paracetamol poisoning, its use in other disorders has only experimental or anecdotal support. For example, in hepatic failure, there are few studies in man showing improved outcome following NAC therapy. There is also conflicting evidence for the use of NAC in sepsis or ARDS and while there is some evidence to suggest that **NAC may be of benefit in acute myocardial infarction**, the patient numbers are small. It may also be of use in ameliorating nitrate tolerance. It is also possible that NAC may confer benefit in reducing the risks of radiographic contrast nephropathy, although the study suggesting this was probably insufficiently powered to review all patient subsets (e.g. diabetics). **N-acetylcysteine would also appear to enhance T cell function in HIV infected patients.** However, the use of **NAC for immunomodulation in HIV patients** has not yet undergone prospective randomised controlled trials and therefore cannot be recommended as routine therapy in HIV infected, or other immune deficient, patients. There is currently insufficient evidence to propose NAC for the treatment of carbon monoxide poisoning. Whilst there is experimental evidence for a variety of novel roles for NAC, further clinical studies are required before it can be recommended for the routine management of any disorders other than that of paracetamol poisoning. CONCLUSIONS: **N-acetylcysteine has antioxidant properties that may be useful in many clinical conditions.** Currently, however, it can only be recommended as therapy for paracetamol poisoning, in all other disorders it is still under evaluation.

**[Effect of thiol antioxidant on body fat and insulin reactivity]**

Division of Immunochemistry, Deutsches Krebsforschungszentrum, Im Neuenheimer Feld 280, 69120 Heidelberg, Germany. J Mol Med. 2004 May; 82(5): 336-44.

Insulin signaling is enhanced by moderate concentrations of reactive oxygen species (ROS) and suppressed by persistent exposure to ROS. **Diabetic patients show abnormally high ROS levels and a decrease in insulin reactivity which is ameliorated by antioxidants, such as N-acetylcysteine (NAC).** A similar effect of NAC has not been reported for non-diabetic subjects. We now show that the insulin receptor (IR) kinase is inhibited in cell culture by physiologic concentrations of cysteine. In two double-blind trials involving a total of 140 non-diabetic subjects we found furthermore that NAC increased the HOMA-R index (derived from the fasting insulin and glucose concentrations) in smokers and obese patients, but not in nonobese non-smokers. In obese patients NAC also caused a decrease in glucose tolerance and body fat mass. Simultaneous treatment with creatine, a metabolite utilized by skeletal muscle and brain for the interconversion of ADP and ATP, reversed the NAC-mediated increase in HOMA-R index and the decrease in glucose tolerance without preventing the decrease in body fat. As the obese and hyperlipidemic patients had lower plasma thiol concentrations than the normolipidemic subjects, our results suggest that low thiol levels facilitate the development of obesity. Supplementation of thiols plus creatine may reduce body fat without compromising glucose tolerance.

**[Potentially fatal paracetamol overdose and successful treatment with 3 days of intravenous N-acetylcysteine regime-- a case report]**

Department of General Medicine, Tan Tock Seng Hospital, Singapore. *Ann Acad Med Singapore*. 2006 Feb;35(2):108-11

**INTRODUCTION:** Paracetamol overdose is the most common drug overdose worldwide. To our knowledge, the maximum number of paracetamol tablets ingested reported in the literature is 45 g. **CLINICAL PICTURE:** We describe a 21-year-old patient who acutely ingested 120 tablets, each 500 mg paracetamol (i.e., 60 g equivalent to 1200 mg/kg body weight) in a suicidal attempt. Our patient also drank 2 bottles of codeine-based cough syrup equivalent to 360 mg of codeine. At 6 hours post ingestion, her serum paracetamol level was 207 mg/L. The poor prognostic factors for paracetamol overdose in our patient included massive paracetamol ingestion (confirmed by blood levels), codeine co-ingestion and elevated serum amylase (189 U/L). **TREATMENT:** She was treated with a 3-day modified regimen of intravenous N-acetylcysteine. **OUTCOME:** The liver function tests and the prothrombin time remained normal over the second and third day of admission and the patient was discharged without complications on the fifth day. **CONCLUSION:** From this experience we feel that in very severe paracetamol poisoning, a modified regime of **intravenous N-acetylcysteine for 3 days is safe and efficacious.**

**[In vivo hyperoxic preconditioning prevents myocardial infarction by expressing bcl-2]**

Department of Pharmacology, Seoul National University College of Medicine, 28 Yongon-dong, Chongno-gu, Seoul 110-799, Korea. kimmsu@snu.ac.kr. *Exp Biol Med (Maywood)*. 2006 Apr;231(4):463-72

Preconditioning with oxidative stress has been demonstrated in vitro to stimulate the cellular adaptation to subsequent severe oxidative stress. However, it is uncertain whether this preconditioning works in vivo. In the present study, we examined in vivo the beneficial effect of oxidative preconditioning. After rats were **pretreated with whole-body hyperoxygenation (100% O<sub>2</sub>)** at 3 atmosphere for 20 mins, four cycles with 20-min intermission), isolated hearts were subjected to 45-min ischemia followed by 90-min reperfusion. **This hyperoxic preconditioning significantly reduced infarct size**, cytochrome-c release, DNA fragmentation, and terminal deoxynucleotidyl transferase-mediated dUTP nick-end labeling-positive cell frequency in the left ventricle, biphasically with an early (30-min) and a delayed (48-hr) effect after the hyperoxygenation. Mechanistically, the NF-kappaB activity and Bcl-2 expression were enhanced in the hearts, and a NF-kappaB inhibitor, pyrrolidine dithiocarbamate, abolished the Bcl-2 induction as well as the infarct-limiting effect. An antioxidant, N-acetylcysteine, and protein kinase C (PKC) inhibitors chelerythrine and Go 6983 also blocked the preconditioning effects. These results indicate that **hyperoxia induces myocardial tolerance against ischemia-reperfusion injury** in association with Bcl-2 induction by NF-kappaB activation through reactive oxygen species and PKC-dependent signaling pathway.

**[The effect of N-acetylcysteine in combination with vitamin C on the activity of ornithine decarboxylase of lung carcinoma cells - In vitro]**

Department of Biochemistry, University of Madras, Guindy Campus, Chennai-600025, Tamilnadu, India. *Life Sci*. 2006 Mar 6; [Epub ahead of print]

Ornithine decarboxylase (ODC) is a marker of lung cancer and is a key enzyme in the synthesis of polyamines, which are necessary for the promotion of the growth of malignant cells. This study assesses the dose-dependent effect of **N-acetylcysteine (NAC), a chemopreventive agent, in combination with vitamin C (VC)** on the activity of ODC in lung carcinoma cell line, NCI-H82. The cells were subjected to supplementation of NAC and VC both individually and in combination at different dosages for 24 h as well as 48 h. The cells were incubated with radiolabeled L-ornithine (<sup>14</sup>C) after the supplementation of NAC and VC individually as well as in combination. A microprocedure was carried out to estimate the activity of ODC in cells after 24 and 48 h of incubation. The activity which was found to be elevated in control cells was decreased significantly on drug supplementation in dose-dependent fashion. The content of nucleic acids also exhibited similar result and [(3)H]-thymidine incorporation was also affected by the supplementation.

**[High-dose oral N-acetylcysteine, a glutathione prodrug, modulates inflammation in cystic fibrosis]**

\*Departments of Genetics and Pediatrics, Stanford University School of Medicine, Stanford, CA 94305. *Proc Natl Acad Sci U S A*. 2006 Mar 21;103(12):4628-33. Epub 2006 Mar 13

**Neutrophilic airway inflammation is a hallmark of cystic fibrosis (CF).** As high oxidant producers, airway neutrophils contribute largely to the systemic redox imbalance seen in CF. In turn, this chronic and profound imbalance can impact circulating neutrophils before their migration into airways. Indeed, in 18 CF patients with stable disease, blood neutrophils were readily deficient in the pivotal antioxidant glutathione (P = 0.003, compared with 9 healthy controls). In a phase 1 study, this deficiency was improved (P = 0.025) by the glutathione prodrug N-acetylcysteine, given orally in high doses (0.6 to 1.0 g three times daily, for 4 weeks). This treatment was safe and markedly decreased sputum elastase activity (P = 0.006), the strongest predictor of CF pulmonary function. Consistently, neutrophil burden in CF airways was decreased upon treatment (P = 0.003), as was the number of airway neutrophils actively releasing elastase-rich granules (P = 0.005), as measured by flow cytometry. Pulmonary function measures were not improved, as expected with short-term treatment. After excluding data from subjects without baseline airway inflammation, positive treatment effects were more pronounced and included decreased sputum IL-8 levels (P = 0.032). Thus, **high-dose oral N-acetylcysteine has the potential to counter the intertwined redox and inflammatory imbalances in CF.**

**[Focus on antioxidant enzymes and antioxidant strategies in smoking related airway diseases]**

University of Helsinki, Department of Medicine, Pulmonary Division, P O Box 22, Haartmaninkatu 4, Helsinki, FI-00014, Finland. *Thorax*. 2005 Aug;60(8):693-700.

**Cigarette smoke causes significant oxidant stress which is further enhanced by recruitment and activation of inflammatory cells to the lung.** Polymorphisms in some detoxification enzymes are **thought to increase the risk of developing chronic obstructive pulmonary disease (COPD)**, but the ultimate role of genetic variability in antioxidant and/or detoxification enzymes in COPD remains obscure. Some antioxidant enzymes are induced, but the extent of induction is insufficient to protect the lung/alveolar epithelium against cigarette smoke. Exogenous antioxidants such as vitamins do not seem to protect against cigarette smoke related lung injury. **Glutathione related synthetic drugs such as N-acetylcysteine have shown some benefits**, but they may have pro-oxidant side effects. Synthetic compounds with superoxide dismutase and catalase activities have shown promising results in animal models against a variety of oxidant exposures including cigarette smoke in the lung. These results are in agreement with studies highlighting the importance of alveolar antioxidant protection mechanisms in oxidant stress and their

inducibility. These new drugs need to be tested in cigarette smoking related lung injury/inflammation since inflammation/oxidant stress can continue after discontinuation of smoking.

#### [Efficacy of nebulizer therapy with acetylcysteine in outpatients with chronic obstructive lung disease]

[Article in Russian] *Klin Med (Mosk)*. 2005;83(4):59-61

**Chronic obstructive lung disease (COLD) is a widespread illness with constantly growing mortality.** Mucolytic therapy plays a significant role in treatment of patients with COLD. The paper contains the results of **nebulization with acetyl-cysteine** as part of rehabilitation program in outpatients with stable clinical course of I-II stage of COLD. The results demonstrated significant clinical improvement, as well as positive changes in external respiration parameters (1 forced expiratory volume), increase of physical activity tolerance, and disappearance of acute inflammation phase reactants in saliva.

#### [Allyl isothiocyanate and its N-acetylcysteine conjugate suppress metastasis via inhibition of invasion, migration, and matrix metalloproteinase-2/-9 activities in SK-Hep 1 human hepatoma cells]

School of Agricultural Biotechnology and Center for Agricultural Biomaterials, College of Agriculture and Life Sciences, Seoul National University, San 56-1, Shillim-dong, Gwanak-gu, Seoul 151-742, Republic of Korea. *Exp Biol Med (Maywood)*. 2006 Apr;231(4):421-30

**Cruciferous vegetables contain a series of relatively unique secondary metabolites of amino acids, called glucosinolates.** Sinigrin, the predominant aliphatic glucosinolate in cruciferous vegetables, is hydrolyzed to yield allyl isothiocyanate (AITC), which, after absorption and metabolism in humans, is excreted in the urine as an N-acetylcysteine (NAC) conjugate. We have determined the inhibitory effects of AITC and its NAC conjugate on cell proliferation, the expression of matrix metalloproteinases (MMPs), adhesion, invasion, and migration in SK-Hep 1 human hepatoma cells. Our results demonstrate that AITC and NAC-AITC suppress SK-Hep 1 cell proliferation in a dose-dependent manner; by 25% and 30% for 10 microM AITC and 10 microM NAC-AITC, respectively. We examined the influence of AITC and NAC-AITC on the gene expression of MMPs and tissue inhibitors of metalloproteinase (TIMPs). Gelatin zymography also revealed a significant downregulation of MMP-2/-9 expression in SK-Hep1 cells treated with 0.1-5 microM AITC and NAC-AITC compared with controls. Reverse transcriptase polymerase chain reaction revealed dose-dependent decreases in MMP-2/-9 messenger RNA levels in both AITC-treated and NAC-AITC-treated cells. TIMP-1/-2 activities were unaffected by treatment with AITC or NAC-AITC in our experiments. NAC-AITC inhibited cancer cell adhesion and invasion much more potently than its parent compound. NAC-AITC at 5 microM caused excellent inhibition of cell migration for 48 hrs. **These results demonstrate the potential of AITC and NAC-AITC as chemopreventive agents.**

#### [Chemoprevention of genome, transcriptome, and proteome alterations induced by cigarette smoke in rat lung]

Department of Health Sciences, University of Genoa, Via A. Pastore 1, I-16132 Genoa, Italy. *Eur J Cancer*. 2005 Sep;41(13):1864-74

Post-genomic methodologies have provided novel tools for evaluating safety and efficacy of cancer **chemopreventive agents.** We exposed rats to environmental cigarette smoke (ECS) for 28 days, with or without oral administration of **N-acetylcysteine (NAC).** As assessed by 32P-postlabelling, ECS caused a 10-fold increase of DNA adduct levels, which were significantly reduced by NAC. Of 518 proteins tested by antibody microarray, ECS stimulated 56 activities involved in stress response, protein removal, cell replication, apoptosis, phagocytosis, and immune response. NAC alone did not change the amounts of any protein, whereas it significantly decreased the amounts of 6 ECS-induced proteins. The intensity of expression of 278 related genes, assessed by cDNA microarray, was significantly correlated with protein amounts. These observed molecular alterations, which can be attenuated by NAC, represent in part adaptive responses and in part reflect mechanisms contributing to the pathogenesis of smoke-related diseases, including lung cancer, asthma, chronic bronchitis, and emphysema.

#### [N-acetyl-cysteine accelerates transfer of diabetes into non-obese diabetic scid mice]

Keio University School of Medicine, Tokyo, Japan. *Diabetologia*. 2004 Oct;47(10):1803-9. Epub 2004 Oct 22

AIMS/HYPOTHESIS: Type 1 diabetes mellitus is caused by autoimmune pancreatic beta cell destruction, and the destructive process involves several molecular mechanisms including oxygen-reactive species. A cysteine derivative, **N-acetyl-cysteine, is widely used as an antioxidant, but the role of N-acetyl-cysteine in the protection of pancreatic beta cells in type 1 diabetes remains unclear.** The aim of this study was to clarify the effect of N-acetyl-cysteine on beta cells using an adoptive transfer system in a murine model of type 1 diabetes. METHODS: Splenocytes from diabetic female non-obese diabetic mice were transferred into female non-obese diabetic scid/scid recipients to induce diabetes. Just after transfer, N-acetyl-cysteine was administered to non-obese diabetic scid recipients. Two weeks after transfer, the pancreas of the recipients was examined histologically, and cytokine mRNA expression in the pancreas was analysed. In vitro, CD4-positive splenocytes from diabetic donor mice were stimulated with anti-CD3 and anti-CD28 antibodies with or without N-acetyl-cysteine. RESULTS: **Treatment with N-acetyl-cysteine significantly accelerated the transfer of diabetes into non-obese diabetic scid recipients.** Treatment with N-acetyl-cysteine accelerated the infiltration of mononuclear cells accompanied by CD8-positive cells into the intra-islet region of the recipient's pancreas, and enhanced interferon-gamma mRNA expression in the pancreas. In vitro, treatment with N-acetyl-cysteine enhanced interferon-gamma and interleukin-2 production by CD4-positive splenocytes of the diabetic donor mice. CONCLUSIONS/INTERPRETATION: **N-acetyl-cysteine accelerates the transfer of diabetes into non-obese diabetic scid mice and this effect is accompanied by the promotion of local infiltration and T-helper cell type 1 responses.**