Inhibition of NADPH Oxidase as a Strategy for Managing Asthma

Activation of NADPH oxidase plays a mediating role in many phases of asthmatic inflammation: activation of mast cells (enabling secretion of histamine and production of leukotrienes),\(^1\)\(^-\)\(^3\) VCAM-mediated migration of eosinophils into lung tissue,\(^4\) pro-inflammatory activity of eosinophils and neutrophils,\(^5\)\(^-\)\(^7\) and the hyperproliferation of airway smooth muscle cells that contributes to lung remodeling in chronic asthma.\(^8\)\(^,\)\(^9\) NADPH oxidase would also be expected to play a role in the fibrotic response to chronic asthma.\(^10\)\(^-\)\(^12\) Patients with asthma appear to be under increased oxidant stress, with reduced plasma levels of oxidant scavengers.\(^13\)\(^-\)\(^18\) Bilirubin, recently revealed to function as a physiological inhibitor of NADPH oxidase,\(^19\)\(^-\)\(^22\) has been shown to inhibit the migration of eosinophils and lymphocytes into lung parenchyma in asthmatic mice,\(^23\) and to inhibit proliferation of airway smooth muscle cells in vitro.\(^24\) Remission of severe chronic asthma was noted in a patient during an episode of hyperbilirubinemia associated with hepatitis.\(^25\) Inhalation of apocynin, another inhibitor of NADPH oxidase, suppresses the hyperreactive response to methacholine induced by ozone inhalation.\(^26\) Many authorities suggest that antioxidants may have potential in the management of asthma.\(^15\)\(^-\)\(^17\),\(^25\) All of these considerations suggest that bilins (biliverdin, phycocyanobilin),\(^22\) as well as ingestion of spirulina (the richest natural source of phycocyanobilin),\(^27\) may be useful for treating both the acute and chronic phases of asthma.

References


(12) McCarty MF. Administration of bilins and high-dose biotin may replicate the beneficial impact of heme oxygenase-1 induction on pathogenic fibrosis. *Medical Hypotheses* 2007; submitted for publication.


(14) Joseph BZ, Routes JM, Borish L. Activities of superoxide dismutases and NADPH oxidase in neutrophils obtained from asthmatic and normal donors. *Inflammation* 1993 June;17(3):361-70.


(22) McCarty MF. "Iatrogenic Gilbert syndrome" - a strategy for reducing vascular and cancer risk by increasing plasma unconjugated bilirubin. *Medical Hypotheses* 2007; accepted for publication.


