

Sickle Selections

a quarterly newsletter from the University of Rochester Sickle Cell Program

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Nitric Oxide

The "Nobel Molecule of 1998" may have a role in the treatment of Sickle Cell Disease

Three Americans were awarded the 1998 Nobel Prize in Medicine for discovering the effect of nitric oxide¹ (NO) on a wide variety of bodily actions including dilating blood vessels. This simple molecule with its ability to cause vasodilation has been administered by inhalation in the treatment of neonatal pulmonary hypertensive disorders². The ability of inhaled NO to dilate blood vessels is limited to the lungs because NO binds with hemoglobin on entering the blood stream, neutralizing its vessel-expanding effect. It was this binding to normal hemoglobin that led C. A. Head³ at the Massachusetts General Hospital in Boston to investigate its effect on abnormal hemoglobins. In a report published in the Journal of Clinical Investigation, Head and his colleagues describe the effect of NO on sickle hemoglobin and its potential for treating sickle cell disease.

Head found that incubating blood containing normal hemoglobin (HbA) or sickle hemoglobin (HbS) with varying amounts of NO up to 80 ppm increased the oxygen affinity of HbS while having no effect on the oxygen affinity of HbA.

*Sickling occurs because HbS polymerizes when deoxygenated. Increasing the oxygen affinity of HbS would inhibit polymerization.*⁴

They then had three normal volunteers and nine sickle cell disease patients inhale 80 ppm of NO in air for 45 min. They found that the blood taken from the sickle patients retained oxygen more avidly than it normally would, while the blood from the normal volunteers remained unchanged. The increased oxygen affinity persisted in the sickle patients 60 min after the inhalation of NO was discontinued.

The exact mechanism by which this concentration of NO increases the oxygen affinity of HbS is unknown, but is believed not to involve vasodilation. These researchers plan

a multi-center, randomized double-blind study to determine whether NO can reduce the symptoms of sickle cell crises in patients with the disease.

If follow-up studies prove successful, researchers say someday sickle cell patients may be using NO inhalers to treat their symptoms.

References:

1. Not to be confused with nitrous oxide, "laughing gas".
2. Truog, W.E., *Pediatrics* 1998; 101(4):696
3. Head, C.A., et al., *J Clin Invest* 1997; 100(5):1193
4. Sunshine, H.R., *Nature* 1978; 275:238

Flu Shots

Recommended for Sickle Cell Children

As the winter months approach, so do concerns regarding influenza. The Pediatric Hematology Clinic is recommending that children older than 6 months of age with either sickle cell anemia or thalassemia be immunized in preparation for this winter's influenza season.

According to the Red Book, influenza vaccine may be administered simultaneously with MMR (but at a separate site and with a different syringe), Hemophilus b, pneumococcal and oral poliovirus vaccines. Since both influenza

Annual vaccination is recommended because of declining immunity in the year after vaccination.

and pertussis vaccines in young children can cause febrile reactions, the Red Book recommends that influenza vaccine not be given within 3 days of vaccination with DTP.

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Strong Sickle Program
Offers Help

Regarding treatment contact:

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Regarding laboratory diagnosis, newborn screening and genetic counseling, contact:

Dr. Peter Rowley, Sandra LaBella or Starlene Loader, Division of Genetics 275-4602

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