



## PIC QUESTION OF THE WEEK: 03/21 /05

Q: Is there any evidence supporting the use of  $\beta$ -lactam antibiotics in the treatment of amyotrophic lateral sclerosis (Lou Gehrig's disease)?

A: Amyotrophic lateral sclerosis (ALS) is a disease characterized by progressive degeneration of neurons that give rise to the corticospinal tract and motor cells of the brain stem and spinal cord. The disease is marked by weakness, atrophy, and spastic irritability of muscles. ALS can result in cognitive decline, seizures, and stroke and is often fatal within 3-5 years of diagnosis. ALS appears to be strongly associated with glutamate, an excitatory neurotransmitter. One unique feature of glutamate is its ability to over-stimulate neurons resulting in their death. When motor neurons die, the brain is unable to initiate and control muscle movement. Researchers believe that improving glutamate transport can reduce the risk of excitatory damage to neurons and slow disease progression. Recent studies suggest that  $\beta$ -lactam antibiotics, specifically ceftriaxone (Rocephin®), may be effective in activating glutamate transporters, thereby decreasing levels of glutamate. This was discovered after a comprehensive screening program in which over 1,000 FDA approved drugs were systematically placed on rodent spinal cord cultures to determine their effect on GLT1 (glutamate transporter) expression. A clinical trial to evaluate the effects of ceftriaxone in ALS begins its enrollment of 600 patients in 2005. Earlier anecdotal reports of ceftriaxone use in ALS were inconclusive. Riluzole (Rilutek®) is the only drug currently labeled for the treatment of ALS. It may lengthen the tracheostomy-free period, however, its benefits have been considered only marginal. The drug inhibits pre-synaptic release of glutamate, thus reducing the effects of the neurotransmitter. Unlike ceftriaxone, it is not believed to induce production of new transport proteins.

### References:

- Miller TM, Cleveland DW. Treating neurodegenerative diseases with antibiotics. *Science* 2005;307:361-2.
- Rothstein J, Patel S, Regan M, et al.  $\beta$ -lactam antibiotics offer neuroprotection by increasing glutamate transporter expression. *Nature* 2005;433:73-7.

Abbie L. McGowan and Karen E. Predmore, Pharmacy Clerkship Students