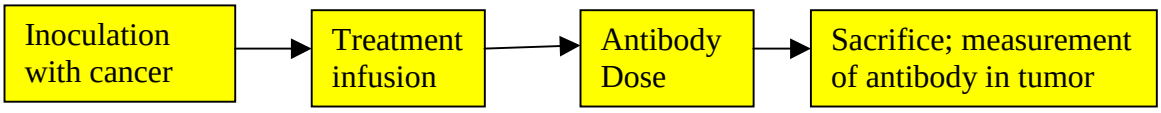
BLOOD-BRAIN BARRIER EXPERIMENT

1. Problem Formulation

The brain is protected from bacteria and toxins, which course through the bloodstream, by a system called the blood-brain barrier. Blood flowing through the brain's capillaries is sealed from outside brain tissue by a single layer of cells. This barrier normally allows only a few substances, including some medications, to reach the brain. Because chemicals used to treat brain cancer have such large molecular size, they cannot pass through the barrier to attack tumor cells. Dr. E. A. Neuwelt from the Oregon Health Sciences University, developed a method of disrupting the barrier by infusing a solution of concentrated sugars.

As a test of the effectiveness of the disruption mechanism, researchers conducted a study on rats. The study was described by P. Barnett et al., "Differential Permeability and Quantitative MR Imaging of a Human Lung Carcinoma Brain Xenograft in the Nude Rat", American Journal of Pathology 146(2), 1995, pages 436-449.

The rats were inoculated with cancer cells to induce brain tumors. After 9 to 11 days they were infused with either the barrier disruption (BD) solution or, as a control, a normal saline (NS) solution. No random mechanism was used to assign the rats to the two treatments. Fifteen minutes later, the rats received a standard dose of the therapeutic antibody L6-$(ab')_2$. After a set time they were sacrificed, and the amounts of antibody in the brain tumor and in normal tissue were measured. The time line for the experiment is shown below:



The data from the experiment are available in the SPSS file brain.sav located in the STAT 252 directory on the FTP server.

The following is a description of the variables in the data file:

Column	Name of Variable	Description of Variable
1	BRAIN	Brain Tumor Antibody Count (per gm)
2	LIVER	Liver Antibody Count (per gm)
3	TIME	Sacrifice Time (hours)
4	TREATMENT	BD if infused with the barrier disruption, NS if infused with a normal saline solution (control)
5	DAYS	Days after inoculation
6	SEX	F= Female, M= Male

7	WEIGHT	Initial weight (grams)
8	LOSS	Weight Loss (grams)
9	TUMOR	Tumor Weight (10^{-4} grams)

We will use SPSS to answer the following questions using the data:

1. Was the antibody concentration in the tumor increased by the use of the blood-brain barrier disruption infusion? If so, by how much?

2. Do the answers to the two questions in 1 depend on the length of time after the infusion (from 1/2 to 72 hours)?

3. What is the effect of treatment on antibody concentration after weight loss, total tumor weight, sex, and initial weight are accounted for?