vention (usually hospitalization for initiation of medication under cardiac monitoring). If left untreated, unstable angina may result in a heart attack and irreversible damage to the heart. The diagnosis of angina is generally based on clinical history, electrocardiograph stress testing (where patients are exercised on a treadmill to look at the effect on their electrocardiogram), and coronary angiography (to look for narrowings in the coronary arteries) (Williams and Stevens 2002).

4.4.3. Time Scaling

The LC_{50} values for different exposure periods are shown in Figure 2-1. Overall the distribution does not seem to argue against a linear relationship between log(concentration) and log(time), and from the data from E.I. du Pont de Nemours and Co. (1981), a value of 2.6 can be calculated for the exponent n from the slope. Regression analysis of all data yielded a value of n = 2.8. However, taking a closer look at the data from this study suggests that the data might be distributed nonlinearly and that the slope decreases with increasing exposure time.

The AEGL-2 and AEGL-3 exposure concentrations were derived from a mathematical model based on the same COHb at the end of the respective exposure periods. These values are also distributed nonlinearly in a log-log plot: the slope between the two shortest exposure periods (10 and 30 min) is equivalent to n = 1.0-1.1, and the slope between the two longest exposure periods (4 and 8 h) is equivalent to n = 2.9-3.4. This nonlinearity is probably caused by the fact that the COHb depends strongly on the ventilation rate and lung blood flow for short exposure rates; for long exposure rates the COHb becomes independent of these parameters and exclusively depends on the affinity of hemoglobin for CO (represented by the Haldane constant M). Because rats have a higher ventilation rate per kilogram of body weight than humans, their COHb concentrations reach the steady state faster, and, therefore, for the same exposure time, the slope for rats is smaller than the corresponding slope for humans, that is, the COHb concentration depends strongly on the ventilation rate in humans compared with rats.

4.4.4. Mathematical Models of COHb Formation

In 1965, Coburn et al. developed a differential equation (CFK model) to describe the major physiologic variables that determine the COHb in blood using data from patients with increased endogenous production of CO due to anemia (Coburn et al. 1965). The CFK model is represented by the following equation:

$$\frac{d(COHb)_t}{dt} = \frac{V_{CO}}{Vb} - \frac{COHb_t * P_{O2}}{M * B * Vb * OHb} + \frac{P_{CO}}{B * Vb}$$