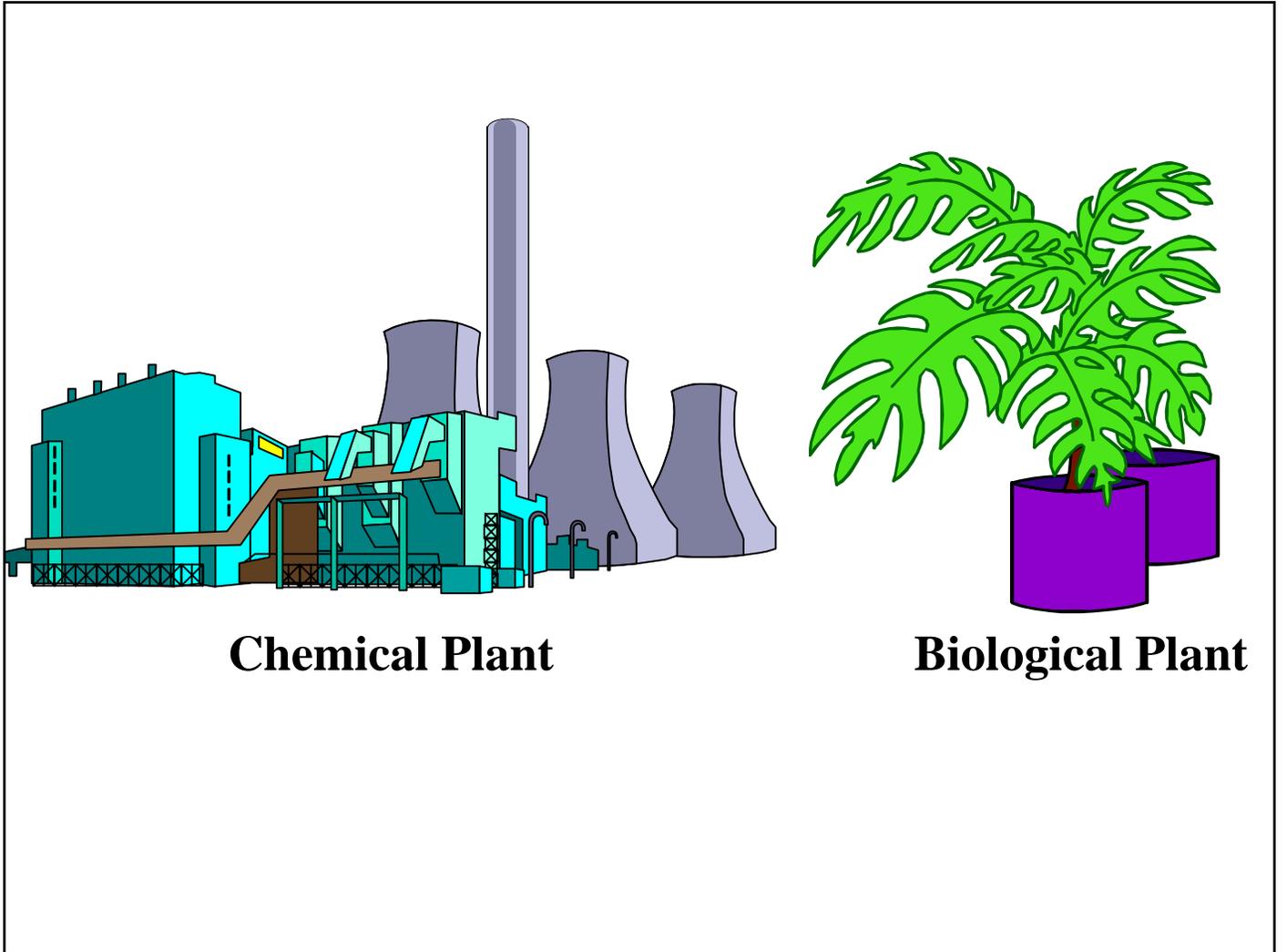


# **Animal Scale-Up**

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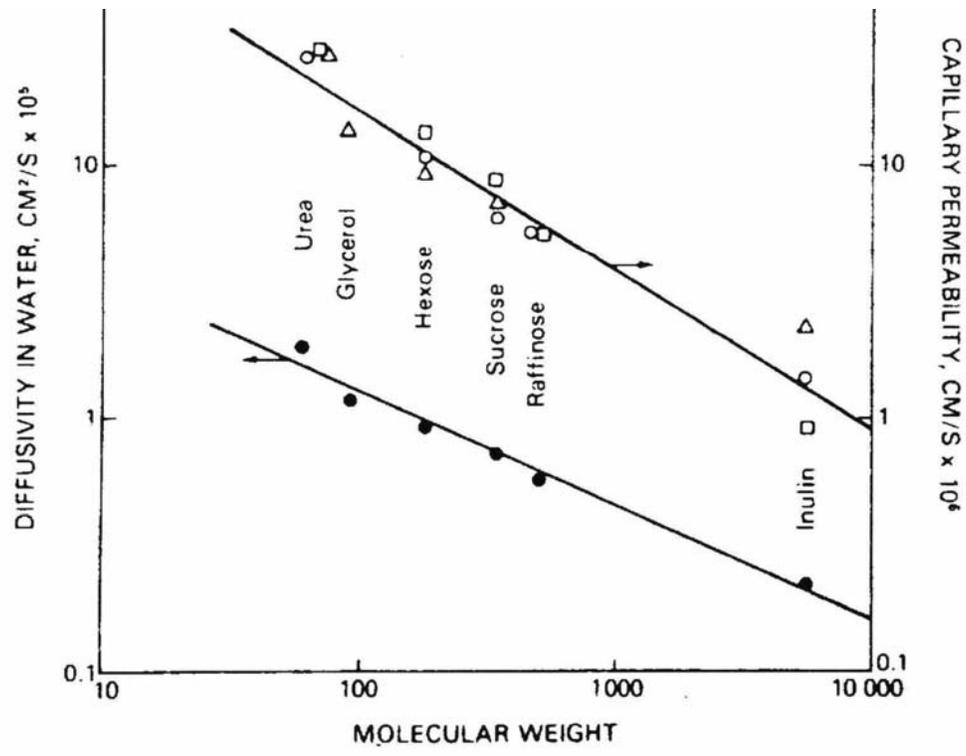












*Capillary permeability and aqueous diffusivity of hydrophilic solutes versus molecular weight. Key: (O) cat leg; (□) human forearm; (Δ) dog heart; (●) diffusivity*

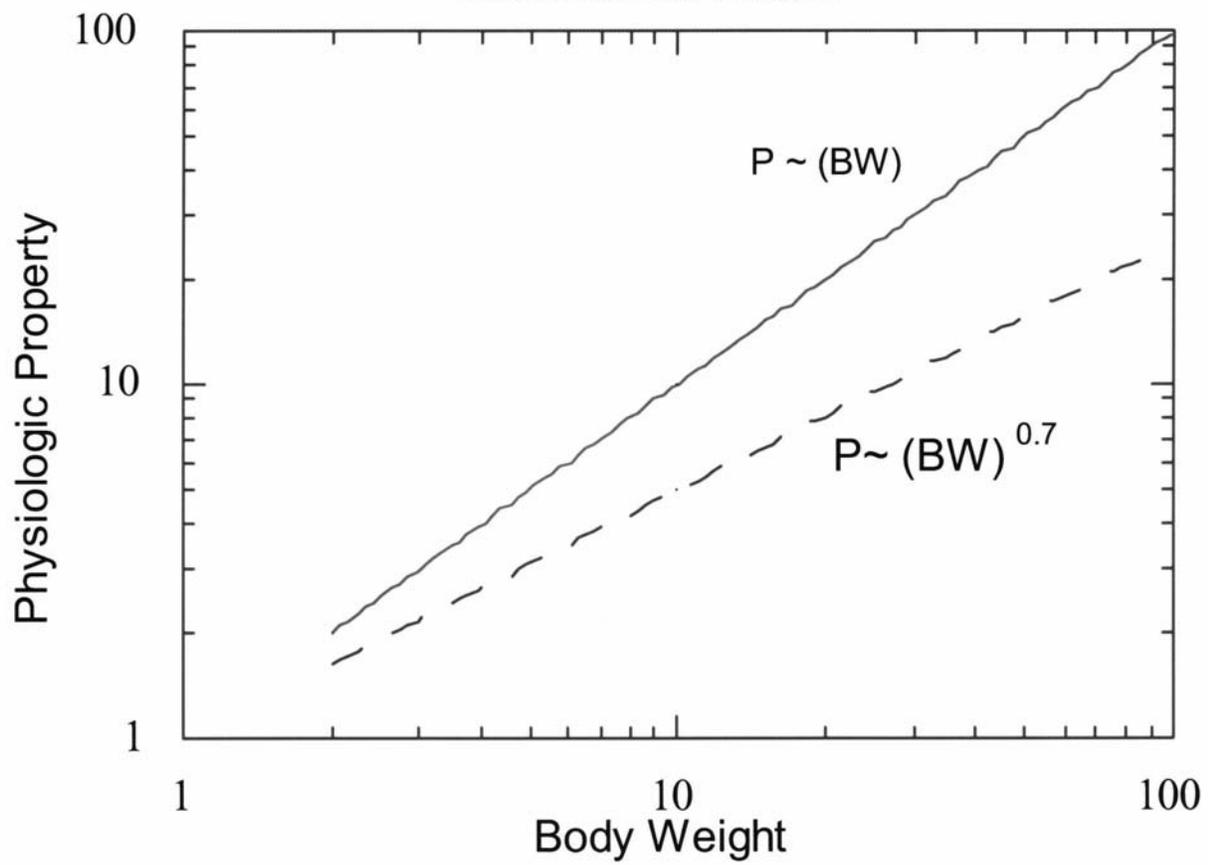
Dedrick RL et al, ASAIO J 5:1-8, 1982

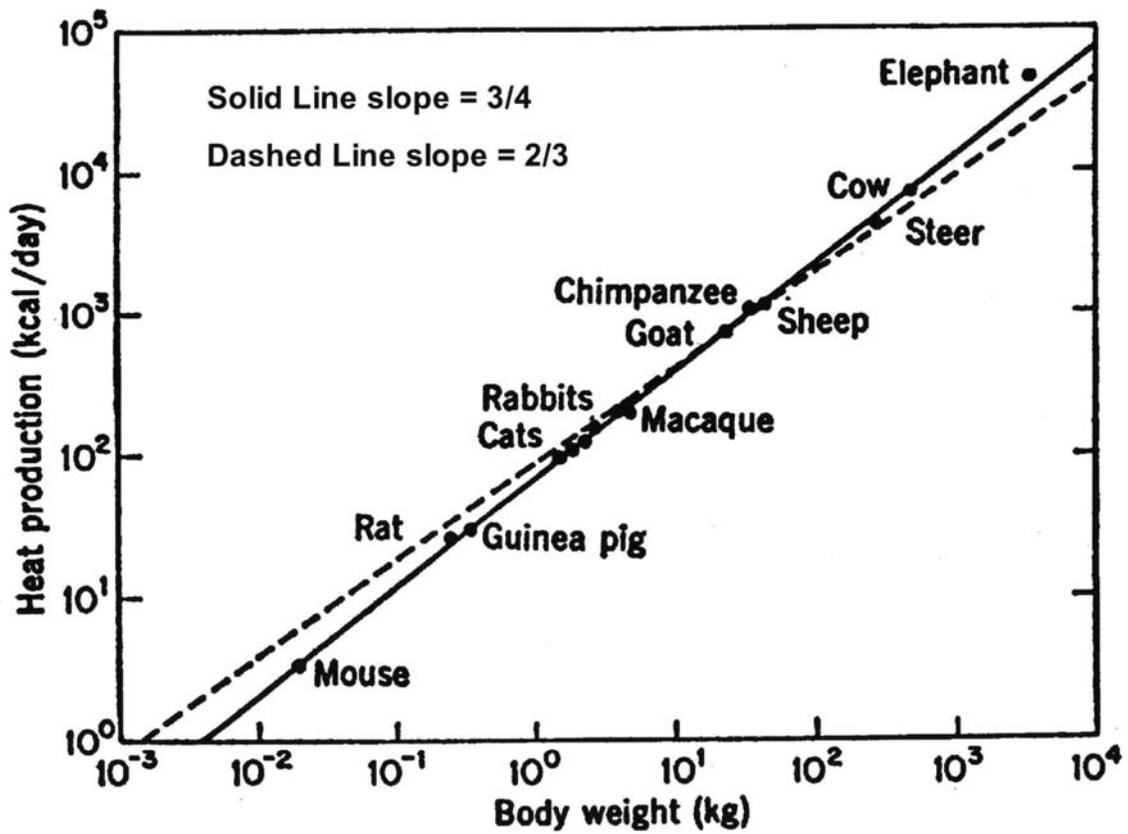
## ALLOMETRIC EQUATION

$$P = a(BW)^m$$

where P = physiological property or anatomic size  
a = empirical coefficient  
BW = body weight  
m = allometric exponent

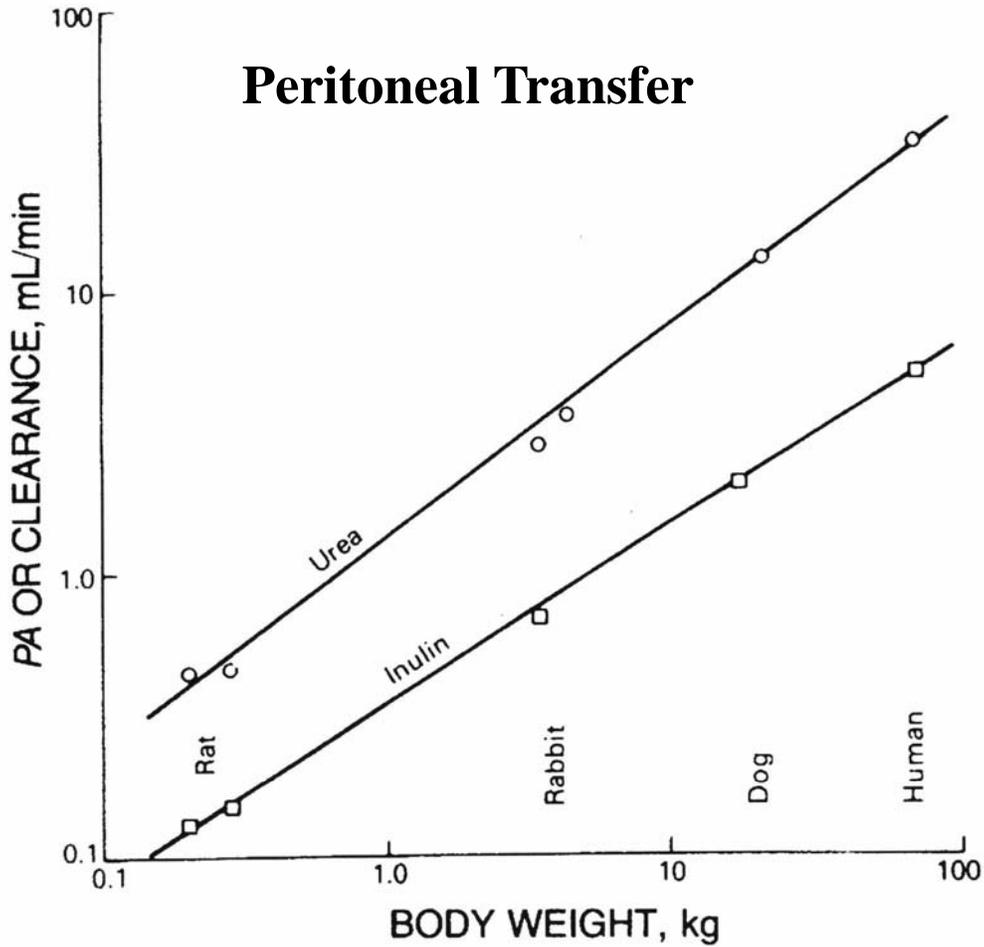
### Allometric Chart



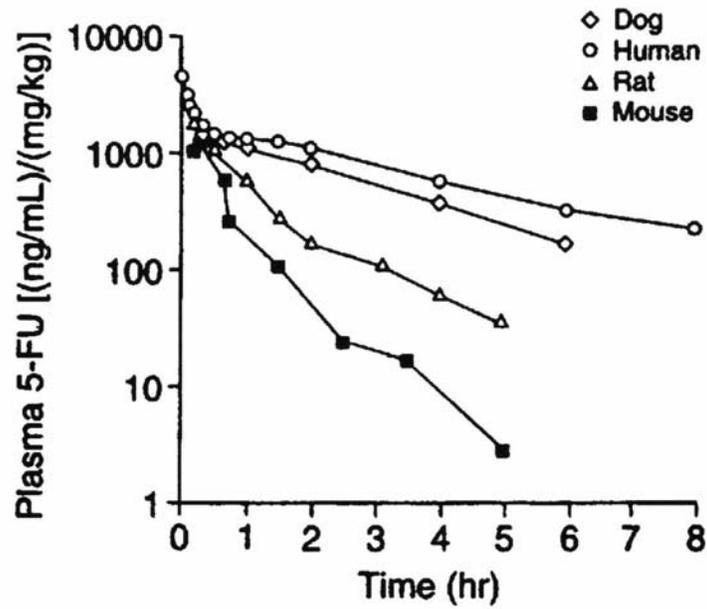


McMahon T. Science 179:1201-1204, 1973

# Peritoneal Transfer

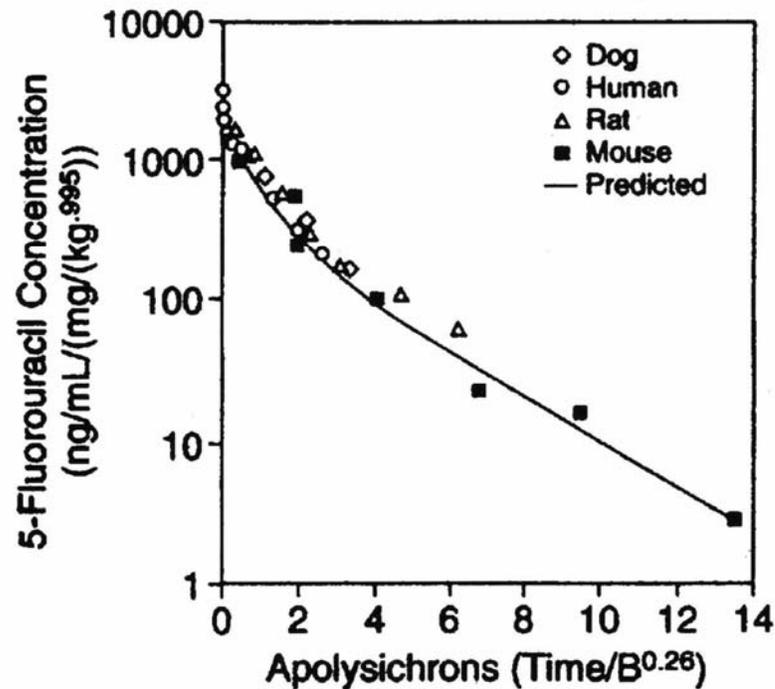


Dedrick RL et al, ASAIO J 5:1-8, 1982



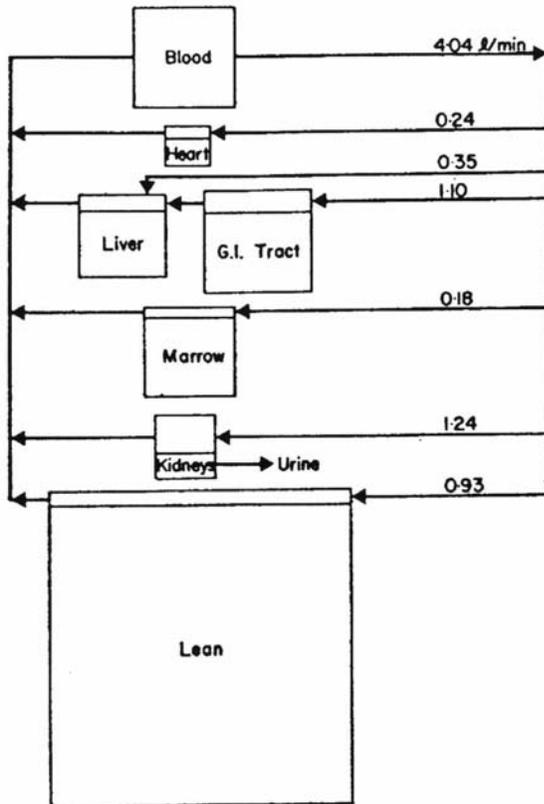
**Dose-normalized plasma 5-FU concentrations in humans and animals lacking dihydropyrimidine dehydrogenase activity. The human data were obtained from a patient who was genetically deficient in DPD. The animals were treated with 776C85 to induce the DPD-deficient state**

Khor SP et al. Cancer Chemother Pharmacol 39:233-238, 1997



Complex Dedrick plot of 5-FU in humans and different animal species with DPD deficiency. The human data were obtained from a patient who was genetically deficient in DPD. The animals were treated with 776C85 to induce the DPD-deficient state

Khor SP et al. Cancer Chemother Pharmacol 39:233-238, 1997



**Compartmental Model for Ara-C Pharmacokinetics**

Dedrick RL et al, Biochem Pharmacol 21:1-16, 1972

### MASS BALANCE EQUATION

$$V_K \frac{dC_K}{dt} = Q_K C_B - Q_K C_K - CL_K C_B - \left( \frac{v_{\max, K} C_K}{K_{m, K} + C_K} \right) V_K$$

where  $V$  = compartment volume, ml

$C$  = drug concentration,  $\mu\text{g/ml}$

$t$  = time, min

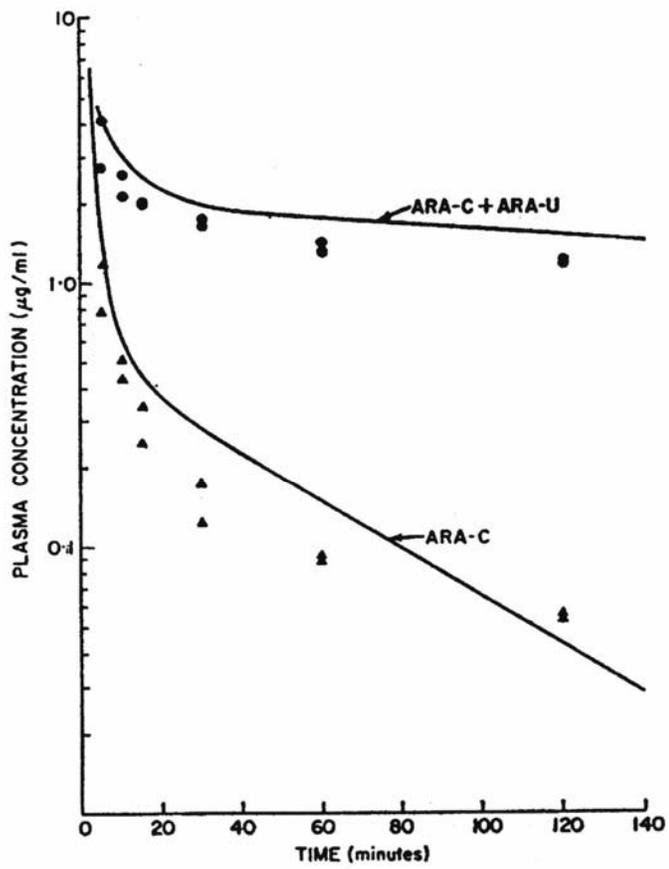
$Q$  = blood flow rate, ml/min

$v_{\max}$  = maximum rate of metabolism,  $\mu\text{g/min ml}$

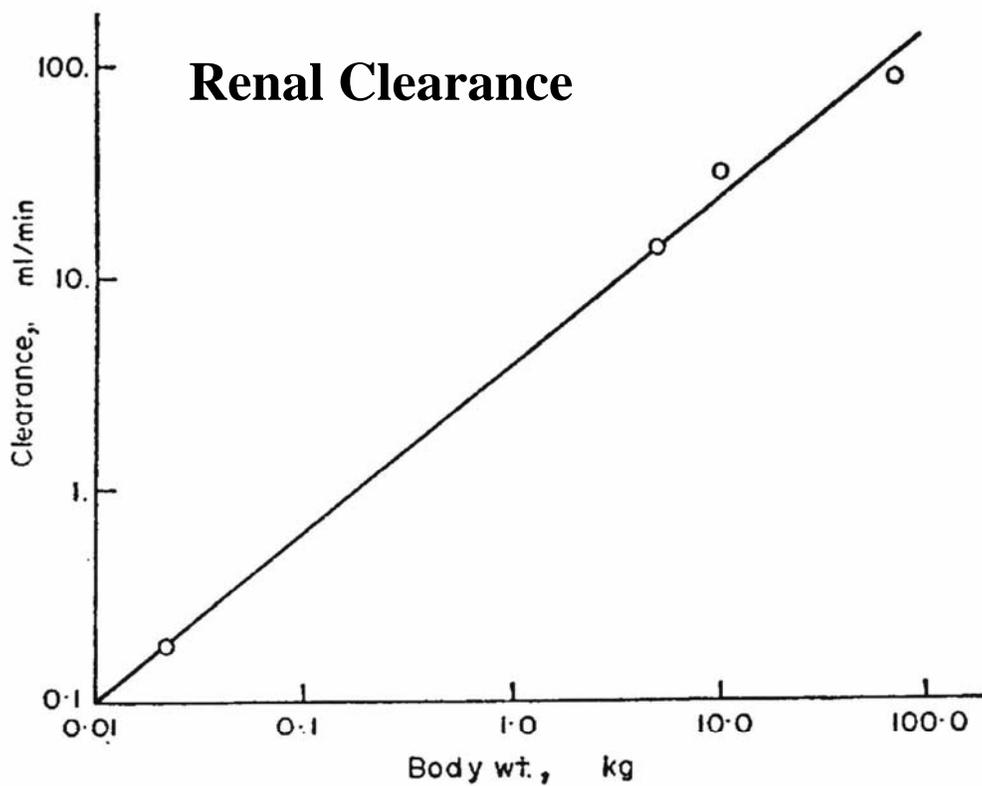
$K$  = Michaelis constant,  $\mu\text{g/ml}$

$CL$  = non-metabolic clearance, ml/min

and the subscripts K and B refer to kidney and arterial blood, respectively.

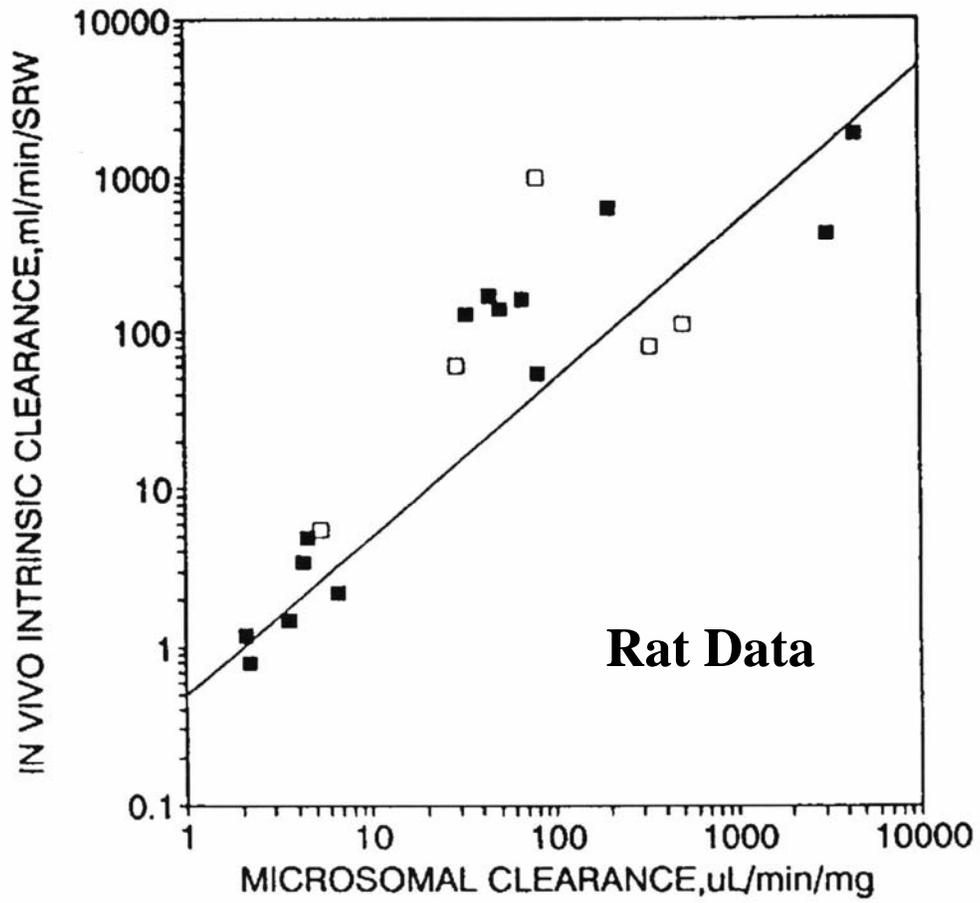


Dedrick RL et al, Biochem Pharmacol 21:1-16, 1972

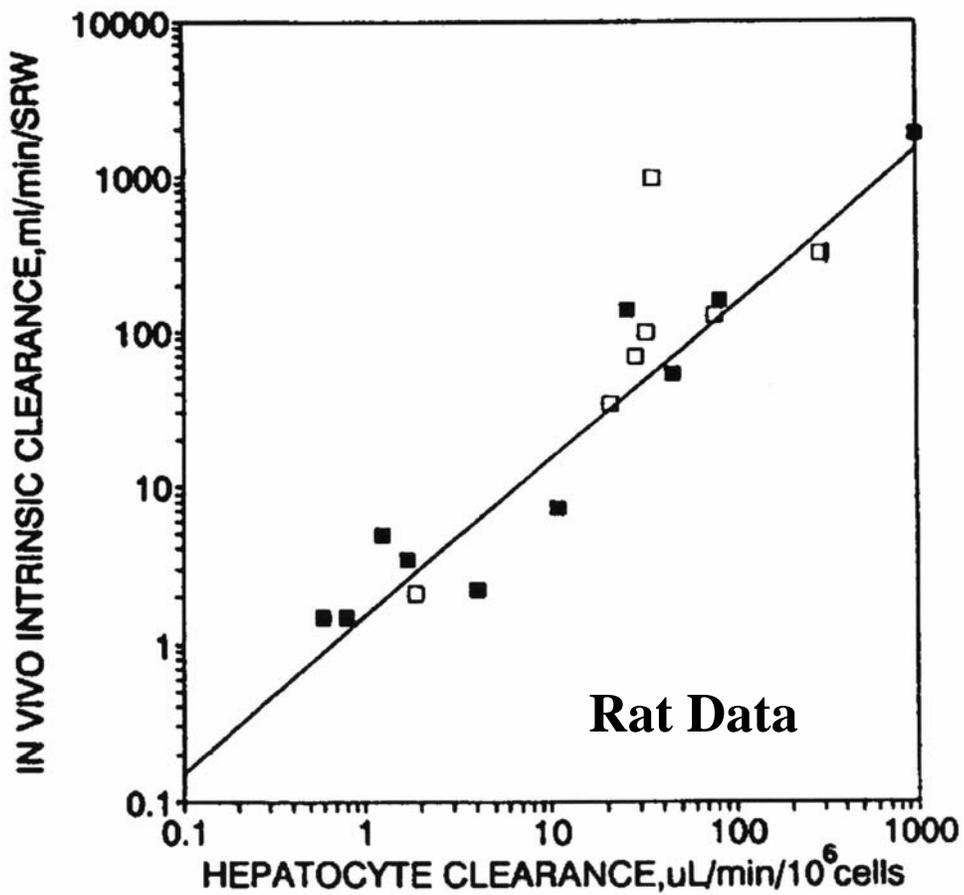


**Kidney clearance of Ara-C and Ara-U vs body weight  
for mice, monkeys, dogs and humans**

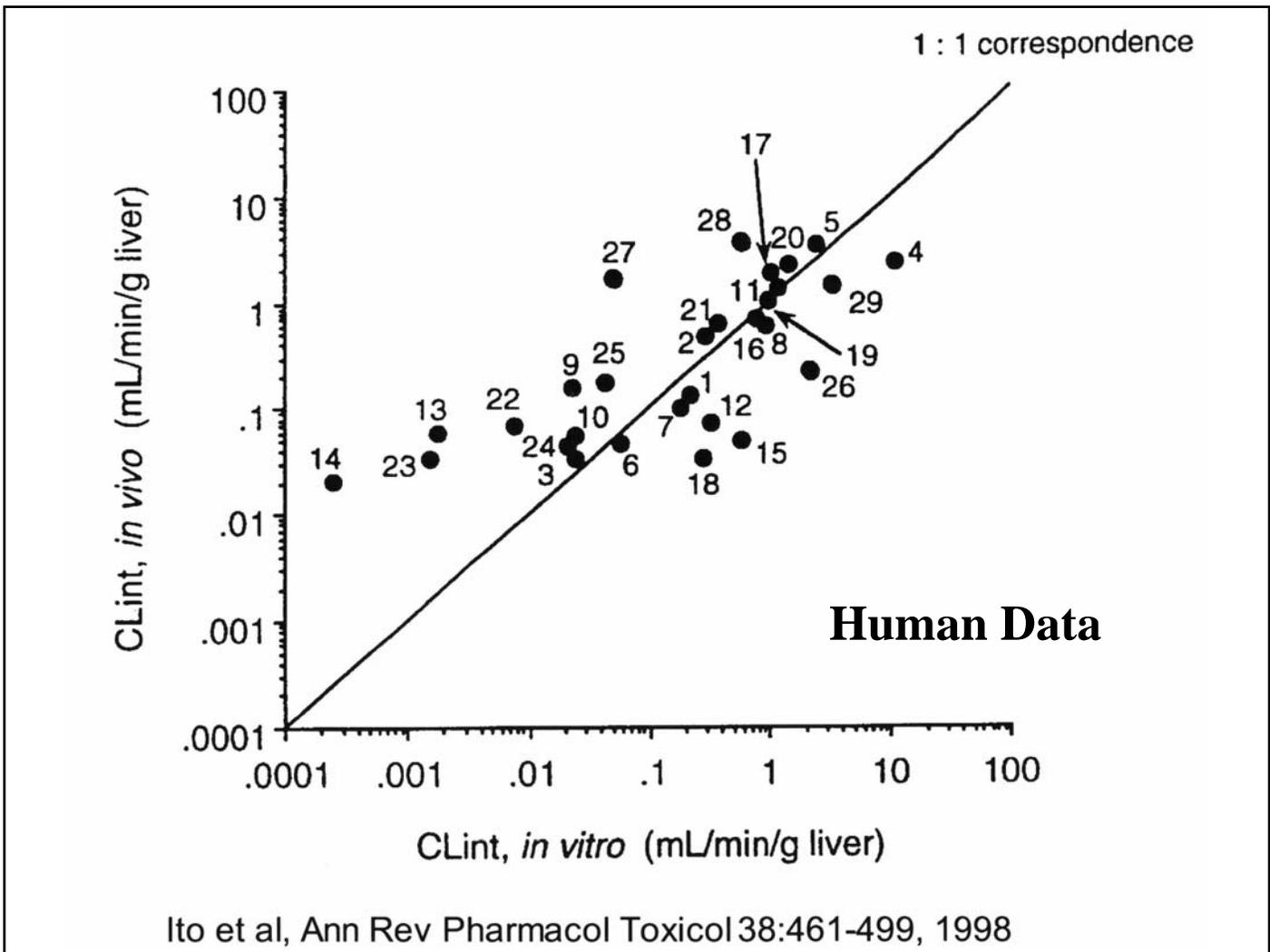
Dedrick RL et al, *Biochem Pharmacol* 22:2405-2417, 1973



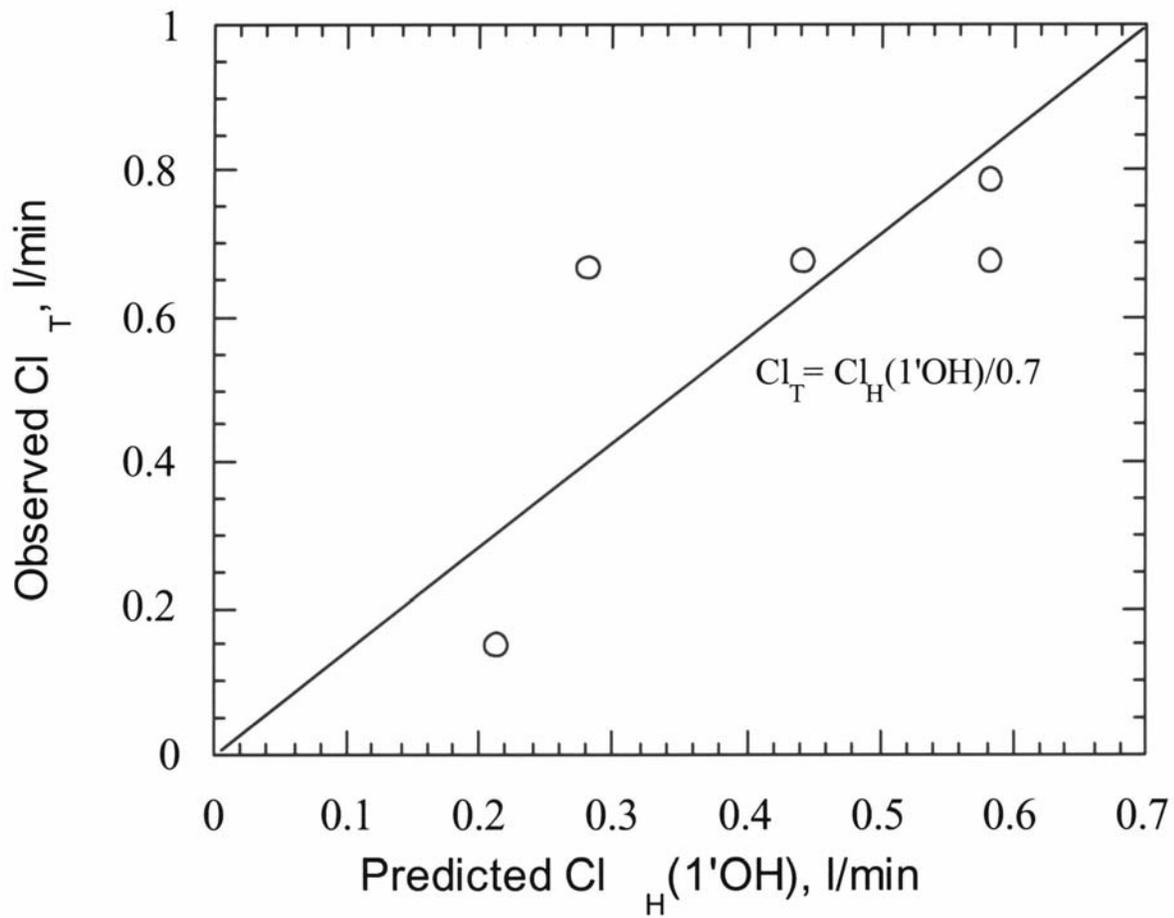
Houston JB, Biochem Pharmacol 47:1469-1479, 1994



Houston JB, Biochem Pharmacol 47:1469-1479, 1994



### Midazolam Clearance Human/Transplant



Data from Thummel et al, J PET 271:549-556, 1994.