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Relationship Between Hg^{203} Excretion Rate and Diuretic Response Following Hg^{203} Mercaptomerin Sodium Administration[1]

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The relationship between the time course of absorption, metabolism, and excretion of a drug and the time course of pharmacologic effects due to the drug is of considerable importance in chemotherapy since dosage regimen and dosage form design are based, in part, on the nature of this relationship. These considerations have led to a re-examination of some of the data reported recently by Calesnick and Wase (1), who determined the average urinary volume and the average excretion of radiomercury at various times after subcutaneous injection of Hg^{203} mercaptomerin sodium. Calesnick and Wase concluded that a dissociated relationship exists between Hg^{203} excretion and the diuretic response. This conclusion was based on a comparison of the time course of diuresis with the time course of Hg^{203} *concentration* in the urine.

A comparison of the time course of diuresis with the time course of Hg^{203} *excretion rate* (concentration x volume) leads to an additional and important conclusion. A plot of average Hg^{203} excretion (cpm per minute) versus average urine flow rate (ml per minute), shown as Figure 1, yields a straight line. This is particularly evident from the points representing the post-equilibrative (post-absorption) phase of the experiment. Interestingly, the straight line intercepts the urine flow rate axis at 1.17 ml per minute, which is about the usual average flow rate of a normal adult human (2). The regression equation calculated from the experimental data (excluding the one point which deviates considerably from the linear relationship) is:

Urine flow rate = 0.84 Hg^{203} excretion rate + 1.17 ml. when urine flow rate is expressed in ml/min, and Hg^{203} excretion rate in cpm/min. Deviations from this type of relationship can be expected to occur upon administration of very large doses, since these probably cause crystalluria (3) by a mechanism analogous to that described with respect to other agents (4). Crystalluria caused by exceeding the solubility of the drug or its metabolites in the urine can affect both urine flow rate and drug (and/or metabolite) excretion rate.

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The present analysis of the data of Calesnick and Wase (1) indicates a definite time intensity relationship between diuresis and Hg^{203} excretion due to Hg^{203} mercaptomerin.

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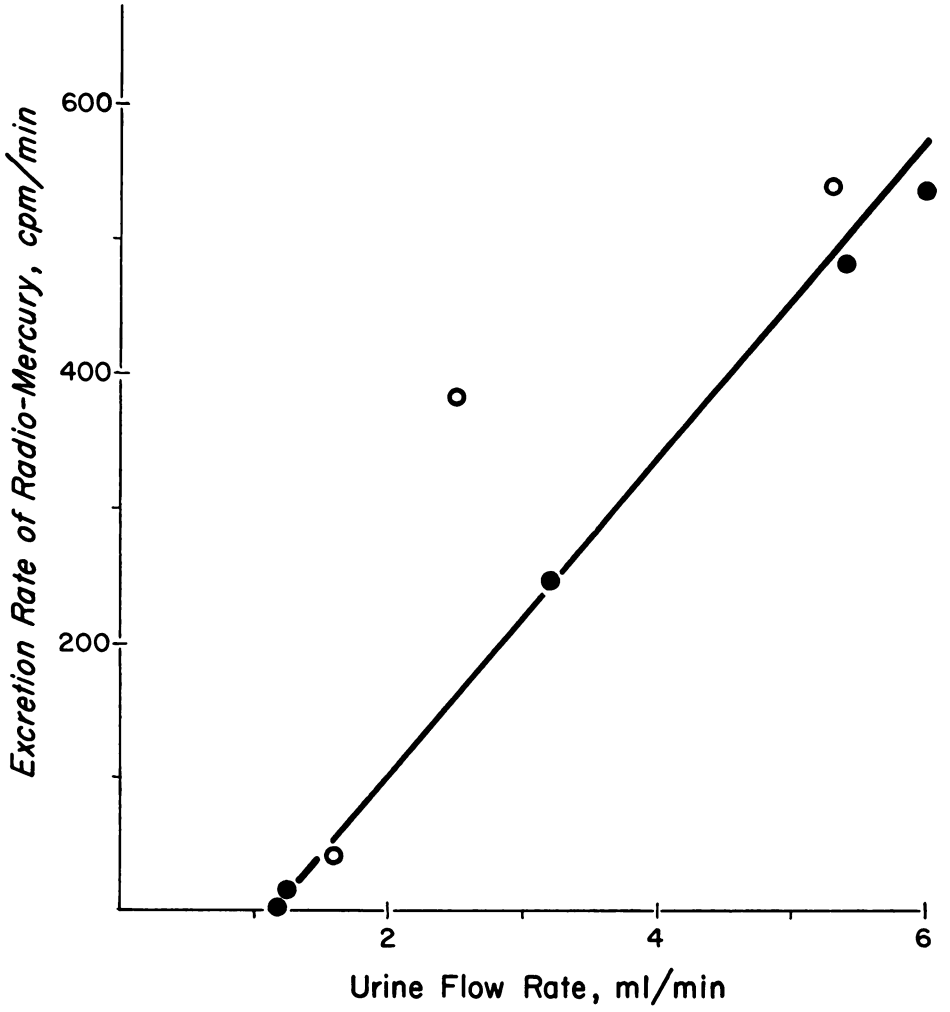

Fig. 1:—Plot of average Hg^{203} excretion rate versus average urine flow rate at various times after subcutaneous injection of Hg^{203} mercaptomerin sodium. Calculated from the data of Calesnick and Wase (1). ○ Absorption phase (up to 175 minutes after drug adminstration), ● post-absorption phase (175 minutes and later after drug administration).