Metabolism and Excretion The metabolic fate of a particular agent largely depends on the chemical linkage between the aromatic residue and the rest of the molecule.Alternatively, severe hepatic disease or reduced hepatic blood flow may produce systemic intolerance to lidocaine and presumably other local anesthetics dependent on adequate liver function for their metabolism.The rapid bio- transformation of articaine to articainic acid (an essentially inactive metabolite) coupled with an unusually extensive tissue distribution significantly reduces the potential for cumulative toxicity after repeat dosing.78 Some local anesthetic metabolites retain significant phar- macologic activity and may contribute to drug toxicity.The initial reaction is usually N-dealkylation of the tertiary amino terminus, principally by CYP3A4 and CYP1A2.64,89 The resultant secondary amine of most amides is susceptible to hydrolysis by hepatic amidase activity, but conjugation, hydroxylation, and further dealkylation may also occur.Much of the sedative effect of lidocaine has been attributed to its de-ethylated metabolites monoethylglycinexylidide and gly- cinexylidide.82 As with the ester compounds, minimal amounts (1% to 20%) of administered amides appear in the urine as unmetabolized compounds.Hepatic blood flow seems to be the rate-limiting factor gov- erning metabolism of lidocaine and some other amides; elimi- nation half-lives range .from 1.5 to 3.5 hours