The paper describes an assay in which histamine was converted to its radiolabeled metabolite, \(^{3}H\)histamine, with histamine-N-methyltransferase and the methyl donor, S-adenosylmethionine-[\(^{14}C\)]methyl ([\(^{14}C\)SAMe]. The precision of the assay was increased by inclusion of [\(\beta\)-side chain label]-\(^{3}H\)histamine as an internal standard and unlabeled methylhistamine as a carrier. The utility of the assay was demonstrated for a wide range of animal and human tissues. [The SCF indicates that this paper has been cited in more than 380 publications.]

### Histamine Revisited

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While a postdoctoral fellow in the Laboratory of Chemical Pharmacology, the Laboratory Chief, Bernard (Steve) B. Brodie, sparked my interest in histamine and the use of isotopes in research. In those days (1966) histamine was known to be localized in granules of tissue mast cells and blood basophils and to be released by chemicals such as compound 48/80 as well as by antigens. There was, however, a 48/80-resistant pool of histamine in most tissues. My task was to measure and determine the role of this “nonmast cell” histamine, which is now known to be located in 48/80-resistant mucosal mast cells and neurons. The limitations of available fluorimetric assays for histamine were becoming evident but a radioenzymatic assay of biogenic amines, devised by Julie Axelrod and his colleagues, was one of several assays for biogenic amines, including the discovery that kidneys from three rats provided sufficient enzyme for one year, were incorporated in an updated version of the assay that was now sufficiently sensitive to measure histamine directly in 10 µl plasma. As the focus of our work shifted to studies of mechanisms of histamine release in vitro, we initially used the assay, but have since turned to simpler alternatives (e.g., measurement of hexosaminidase release) for monitoring degranulation of mast cells. So the incentive for further refinement passed to others as discussed in a recent review. The reason for the high citation of this and the update was, I suspect, because the assay was needed. In fact both enzyme and [\(^{14}C\)SAMe are now sold as a kit by New England Nuclear Corp. Also, the detailed commentaries in the paper ensured that others could adapt the assay for their own needs.