Abstract. In the ischemic heart, high-energy phosphates are rapidly broken down. We studied the release of AMP catabolites from the isolated perfused rat heart which was temporarily made ischemic or anoxic. We measured the concentration of purine nucleosides and oxypurines with a novel high-pressure liquid chromatographic technique. The postischemic working heart released adenosine, inosine, hypoxanthine, and also substantial amounts of xanthine. The latter could indicate that xanthine oxidase is present in rat heart. Further evidence for the myocardial occurrence of this enzyme was obtained from experiments with hearts perfused retrogradely with allopurinol, an inhibitor of xanthine oxidase. This drug greatly enhanced the release of hypoxanthine, both during normoxic and anoxic perfusions. We conclude that xanthine oxidase could play an essential role in the myocardial breakdown of AMP catabolites.

The myocardial cell needs a variety of nucleotides as precursors of nucleic acids and the nucleotide coenzymes for group transfer and bioenergetic processes. ATP plays a special role in heart muscle because it is the fuel for the pump. Large amounts of oxygen are permanently needed for the production of ATP through oxidative phosphorylation. There is a delicate equilibrium between synthesis and breakdown of ATP. During hypoxia ATP is rapidly dephosphorylated, and adenosine and its catabolites are released from the heart (for review, see ref. 3). We used inosine and hypoxanthine as markers for ischemia in animal models such as the isolated perfused rat heart (12) and the open-chested pig heart preparation (4) and in the clinical setting, during an atrial pacing stress test (11). In these instances, inosine and the combination of hypoxanthine and xanthine were measured with Olsson’s enzymological method (9). We assumed that hypoxanthine was the end product of myocardial adenine nucleotide metabolism.

With a novel high-pressure liquid chromatographic method, we are now able to distinguish between xanthine and hypoxanthine (6) and report here the production of adenosine, inosine, hypoxanthine, and xanthine from the isolated perfused rat heart. Studies with allopurinol indicate that xanthine oxidase (E.C. 1.2.3.2) is present in rat heart.
MATERIALS AND METHODS

The experiments were performed with F₁ hybrid male rats (250–440 g) obtained from two inbred Wistar substrains. The animals were anesthetized with 30 mg pentobarbital i.p. Hearts were quickly excised and arrested in cold perfusion medium, a modified Tyrode solution (2). For our first set of experiments, the working heart preparation developed by Neely and Rovetto (8) was used. For the induction of ischemia, a one-way ball valve was placed in the aortic outflow tract (8). In a second series of experiments,

![Graph showing ischemia-induced rise in coronary purine nucleoside concentration in the isolated working rat heart.](image-url)