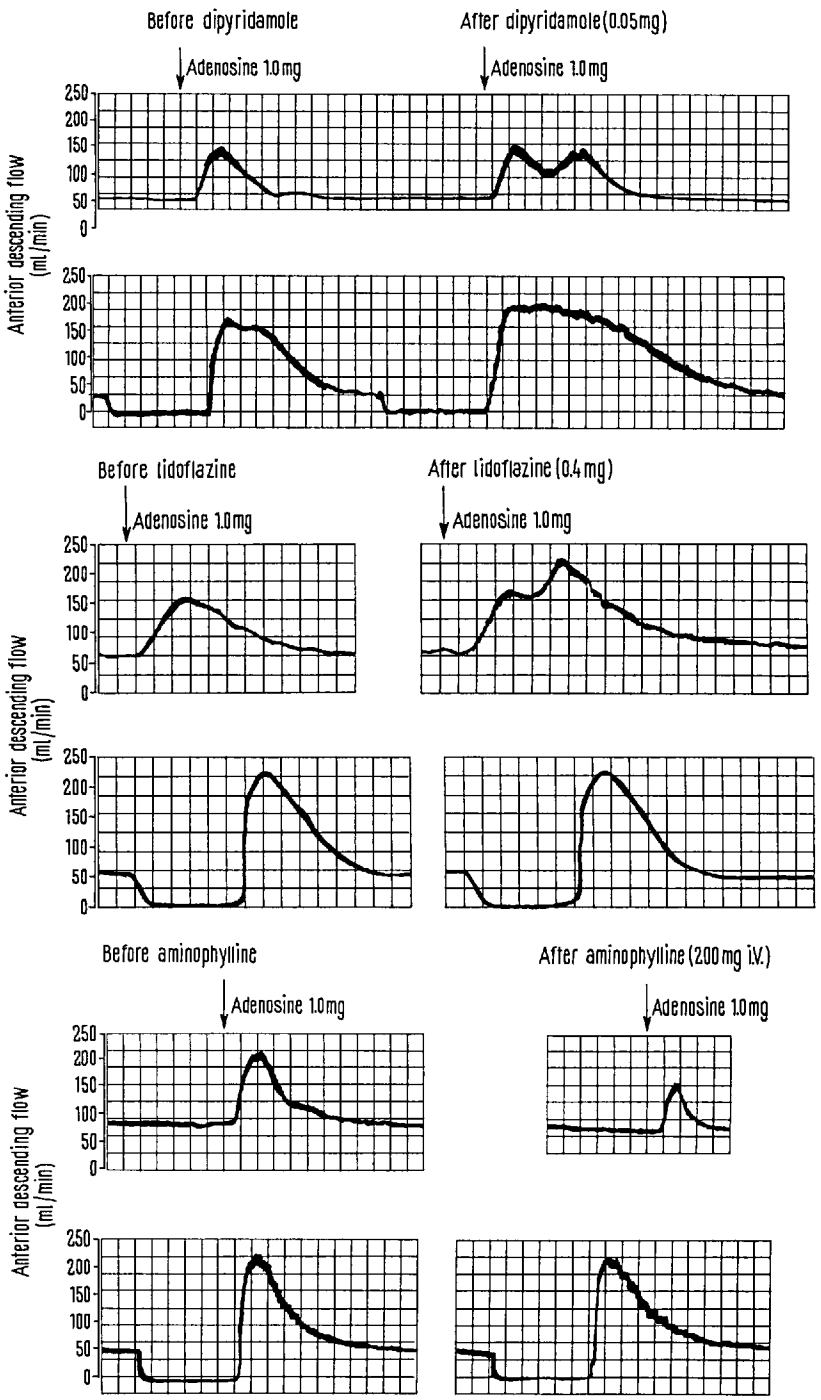
Role of Adenosine in Reactive Hyperemia of the Dog Heart

The concept that reactive hyperemia in heart muscle is caused by vasoactive metabolites[1-3] is supported by the observation that the heart of the dog releases adenosine in the course of reactive hyperemia[4]. The possibility that this phenomenon is due to the liberation of adenosine has now been examined by testing the effect of 3 drugs which are known to produce changes in coronary vasodilatation caused by adenosine. Both dipyridamole[5] and lidoflazine[6,7], markedly enhance adenosine-induced coronary vasodilatation, whereas aminophylline[7] has the opposite effect. It therefore seemed reasonable to see whether prior administration of the first 2 drugs would enhance the reactive hyperemia, while administration of aminophylline would reduce it.

This study involved the use of 33 dogs. They were anesthetized with 3 mg/kg of morphine sulfate s.c. followed in h by i.v. sodium pentobarbital, 7.5 mg/kg, allobarbital 12.5 mg/kg, urethane 150 mg/kg and monoethylurea 50 mg/kg. Ventilation was maintained with a Harvard animal respirator pump using room air. The open chest approach made it possible to expose and suspend the heart in a pericardial cradle. A short segment of the anterior descending branch of the left coronary artery was dissected free and a non-cannulating Biotronex



The effect of the drugs dipyridamole, lidoflazine and aminophylline on adenosine induced coronary vasodilatation and on myocardial reactive hyperemia. All reactive hyperemia responses followed 60 sec occlusions. It can be seen that while the 3 drugs influenced adenosine induced coronary vasodilatation, only dipyridamole modified reactive hyperemia.

flow transducer placed around it for measurement of coronary blood flow. A 1 mm diameter teflon catheter was introduced into a small branch of the anterior descending coronary artery for local injection of drugs. A left atrial catheter was used for adenosine infusions. In the first part of each experiment, it was essential to show that dipyridamole and lidoflazine enhanced adenosine induced coronary vasodilatation, while aminophylline had the opposite effect. This was usually accomplished using the following dosages: dipyridamole 0.05 mg, lidoflazine 0.4 mg (both infused directly into the coronary circulation), aminophylline 200 mg i.v. and 1.0 mg adenosine injected into the left atrium. Reactive hyperemia was produced by temporary 60 sec occlusions of the anterior descending artery. Following control studies, occlusions were repeated after intracoronary administration of either dipyridamole or lidoflazine. Aminophylline was given i.v. All drugs were given in the same dosage as for the adenosine experiments.

The results of these experiments are summarized in the Figure. Following the infusion of dipyridamole, enhancement of both reactive hyperemia and adenosine induced coronary vasodilatation occurred ($p < 0.001$). Lidoflazine enhanced the coronary response to infused adenosine ($p < 0.001$) but no significant change ($p > 0.5$) occurred in the reactive hyperemia response. Although able to diminish adenosine induced vasodilatation ($p < 0.001$), aminophylline failed to produce a change in myocardial reactive hyperemia ($p > 0.3$).

The mechanism by which these drugs influence coronary vasodilatation produced by adenosine is unknown. It has been suggested that dipyridamole and lidoflazine prevent the uptake by the myocardium of infused adenosine[8] and that dipyridamole inhibits the degradation of adenosine in myocardial tissue[9]. These actions might explain the observed effects of these two drugs. Caffeine has been shown to antagonize the cardiac effect of adenosine[10], a property which may well be shared by aminophylline and other xanthines.

The provisional conclusion drawn from these experiments is that myocardial reactive hyperemia in the dog is not solely mediated by adenosine[11].

Résumé. Le dipyridamol, la lidoflazine et l'aminophylline modifient la vasodilatation provoquée par l'adénosine. Le dipyridamol seul augmente l'hyperhémie réactionnelle et les résultats ne confirment pas l'hypothèse que l'adénosine peut être un médiateur de l'hyperhémie réactionnelle.

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Haloforms: Sweet Taste or Smell?

Haloforms are important compounds in elucidating the initial chemistry of sweet taste and 'smell'. Many subjective reports indicate that as a class these compounds taste sweet[1,2], but they also have been reported to have a 'sweet' odor. Thus, there may be some confusion as to whether haloforms taste sweet, smell sweet or both. In this sense haloforms may serve as a focal point for distinguishing the initial chemistry of gustatory and olfactory responses.

The purpose of this report is to separate the gustatory and olfactory responses to haloforms in the absence of one or the other of these sensory modalities. To do this, we have recorded the gustatory and olfactory responses to haloforms of patients with abnormalities of taste, smell or both of these sensory modalities. These patients have either anosmia[3], Type I hyposmia[4], Type II hyposmia with dysosmia and dysgeusia[5,6] or aglycogeusia[7].

The subjects of this study were 1 patient with anosmia (i.e., a patient who was unable to detect or recognize any vapor using primary or accessory areas of olfaction), 5 patients with Type I hyposmia (i.e., patients who were unable to detect or recognize vapors using their primary olfactory area but who had intact accessory areas), 2 patients with Type II hyposmia with dysosmia and dysgeusia (i.e., patients who had quantitatively decreased olfactory acuity at the primary olfactory area with hypogeusia and an associated abhorence toward various odorants and tastants) and 1 patient with aglycogeusia (i.e., a patient who was unable to recognize the taste of any sweet substance).

Detection and recognition thresholds were determined for representatives of each of four taste qualities (NaCl for salt, sucrose for sweet, HCl for sour and urea for bitter) and for chloroform, bromoform and iodoform by a modification of a forced choice, 3 stimulus drop tech-

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