# Indomethacin and acid secretion in the isolated perfused canine stomach

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The isolated canine stomach will not secrete acid with a disc oxygenator in the arterial inflow. Green & Auden (1972) and Kowalewski & Sharf (1971), therefore, used a donor dog to oxygenate the blood perfusing the stomach. A completely isolated perfused preparation of the stomach would have many advantages since a donor dog introduces additional variable factors. The following experiments were devised to investigate why acid secretion is inhibited in the isolated perfused stomach.

Greyhounds of both sexes were anaesthetized with intravenous pentobarbitone (20 mg/kg) after premedication with fentanyl (0.24 mg) and droperidol (12 mg), and heparinized. Blood was drained from the femoral artery into the perfusion circuit. The coeliac artery was clamped and the arterial supply to the stomach was perfused with a pulsatile pump via the splenic artery. A cannula in the portal vein shunted venous blood from the stomach to the femoral vein, thus by-passing the liver. A continuous intra-arterial infusion of histamine acid phosphate (20 μg/min) to the stomach was used to stimulate acid secretion.

The stomach secreted acid continuously only when the oxygenator was by-passed. When it was included in the circuit, acid secretion was abolished and the platelet count fell from about 30,000 to 10,000/mm$^3$. It is possible that platelet aggregates were formed in the oxygenator and caused mechanical and chemical damage (Bø & Hognestad, 1972) to the gastric mucosa. In order to remove the aggregates before isolating and perfusing the stomach, blood was circulated for 1 h from the femoral artery through the perfusion circuit including the oxygenator and back into the femoral vein. When the stomach was isolated and perfused after this preliminary procedure, a large acid output (up to 36 mEq/h) was observed in response to histamine.

However, if the venous outflow which normally returned to the heart and lungs was diverted to the oxygenator to establish complete vascular isolation, there was an exponential fall in secretion. This inhibition could have been caused by the release of prostaglandins and their accumulation in the absence of the lungs. These substances, which are metabolized in the lungs (Ferreira & Vane, 1967), can inhibit gastric secretion (Robert, Phillips & Nezamis, 1968). Therefore indomethacin, which inhibits prostaglandin synthesis, was injected intravenously (10 mg/kg) into the dog 30 min before isolation of the stomach. After vascular isolation, the stomach was removed and placed in a chamber where acid secretion continued for two hours. This suggests that indomethacin prevents prostaglandins from accumulating in the perfusate and inhibiting gastric secretion.

Indomethacin, besides permitting sustained acid secretion, also caused extensive bleeding from the gastric mucosa into the lumen of the stomach. This preparation might be useful not only for studies of gastric secretion, but also to study the mechanisms involved in drug-induced gastric bleeding.

**References**

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