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Aukland K, Bower B F & Berliner R W. Measurement of local blood flow with hydrogen gas. *Circ. Res.* **14**:164-87, 1964.
[Laboratory of Kidney and Electrolyte Metabolism, National Heart Institute, Bethesda, MD]

This article described polarographic measurement of dissolved hydrogen (H_2) gas by platinum electrodes *in vitro* and implanted in tissues. The rate constant of the exponential washout following H_2-inhalation or arterial infusion of H_2-saturated saline gives local blood flow in tissue surrounding the electrode. [The *SCI*® indicates that this paper has been cited in over 400 publications.]

Knut Aukland
Department of Physiology
University of Bergen
N-5000 Bergen
Norway

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In the 1950s it was established that osmotic concentration of urine requires a hyperosmotic renal medulla. The subsequent recognition that vasa recta flow will tend to dissipate the osmotic gradient[1] created a need for methods for measuring medullary blood flow. Working with F. Kiil and J. Krog in Oslo, Norway, I tried using polarographically determined urine oxygen tension as an indicator, but the results were not convincing.

I talked with Robert W. Berliner at the first International Congress of Nephrology in 1960, and he offered me a fellowship at the Kidney and Electrolyte Laboratory at NIH, proposing that we try to quantitate medullary blood flow by measuring H_2-gas uptake by a platinum electrode inserted into the medulla. Delighted by the proposal, I arrived at NIH in the summer of 1962, where I joined postdoc Bruce F. Bower. He was already recording H_2 potentials versus a calomel electrode, as previously used for detecting cardiac shunts. However, the logarithmic relationship to H_2 concentration and the lack of a meaningful baseline created problems. By varying the circuitry we found that the voltmeter response became linear when we reduced the resistance of the electrode circuit. We also discovered that a similar system had been described by Hyman.[2] In spite of long experience with O_2 polarography, it took me many weeks to realize that we were now measuring H_2-oxidation current, or "available H_2," i.e., we were doing H_2 polarography. Although the delay in making this connection was cause for some humility, comfort could be derived from the fact that the vast literature on polarography contained no mention of H_2.

The linearity of the system was simply demonstrated as an exponential washout of H_2 by diffusion from a well-stirred beaker. According to Kety,[3] any homogeneously perfused tissue should behave similarly, as we soon confirmed for the renal cortex and myocardium. After determining the tissue/blood partition coefficient, we could also calculate absolute flow from the washout rate and demonstrate good agreement with directly measured venous outflow. Paradoxically, the method could not give absolute flow in the renal medulla, which was our prime interest, but did provide new information on medullary countercurrent exchange.[4]

Berliner provided continued encouragement and good ideas during his daily visits in the lab. Without warning, he would suddenly appear with his lit cigar in the middle of our bubbling H_2 flasks. Bruce took comfort in saying: "If the lab blows up, we will never know about it." In any case, Bruce left NIH unhurt in the late fall of 1962.

The H_2 method was not much used or cited during its first decade, possibly because external detection of radioactive gases seemed simpler. Its increasing use in many tissues later on presumably reflects growing awareness of the main advantages of the technique: repeatable and simultaneous measurements of blood flow in several strictly localized tissue areas.

The method has been improved in some details: smaller electrodes probably give less tissue trauma; O_2 sensitivity is reduced by a suitable polarizing potential.[5] Local electrolytic generation of H_2 is an interesting idea[6] that deserves further exploration.

1. **Berliner R W, Levinsky N G, Davidson D G & Eden M.** Dilution and concentration of the urine and the action of antidiuretic hormone. *Amer. J. Med.* **24**:730-44, 1958. (Cited 355 times.)
2. **Hyman E S.** Linear system for quantitating hydrogen at a platinum electrode. *Circ. Res.* 9:1093-7, 1961.
3. **Kety S S.** The theory and application of the exchange of inert gas at the lungs and tissues. *Pharmacol. Rev.* 3:1-41, 1951. (Cited 840 times since 1955.)
4. **Aukland K & Berliner R W.** Renal medullary countercurrent system studied with hydrogen gas. *Circ. Res.* **15**:430-42, 1964. (Cited 55 times.)
5. **Aukland K, Kiil F, Kjekshus J & Semb G.** Local myocardial blood flow measured by hydrogen polarography. Distribution and effect of hypoxia. *Acta Physiol. Scand.* 70:99-111, 1967.
6. **Stosseck K, Lubbers D W & Cottin N.** Determination of local blood flow (microflow) by electrochemically generated hydrogen. Construction and application of the measuring probe. *Pflugers Arch.—Eur. J. Physiol.* **348**:225-38, 1974.