The Clinical Usefulness of Hydrogen Gas as an Indicator of Left-to-Right Shunts

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Several indicators have been recommended for the detection of intracardiac left-to-right shunts. The complexity of instrumentation, the difficulties in handling radioactive materials, and the time involved in the sampling required have precluded the general acceptance of any one method as a routine screening procedure. Furthermore, oxygen saturations, as well as methods utilizing radiopaque contrast material, dyes, and even radioactive indicators, may give equivocal results in the presence of very small left-to-right shunts. Therefore, an inexpensive indicator that permits easy administration and rapid detection of small quantities while still in the bloodstream, by a system requiring a minimum of instrumentation, would be of significant value.

Hydrogen gas is such an indicator, easily detected by an intravascularly located platinum-tipped electrode catheter, which because of its affinity for hydrogen molecules will serve as a hydrogen electrode. Hydrogen, after leaving the alveolar space, is carried in gas form. Upon contact with platinum a partial change from the molecular to the ionic state occurs with the simultaneous release of electrons (\(H_2 \rightarrow 2H^+ + 2e^-\)). The electrical potential obtained from such an electrode is a function of the partial pressure of hydrogen in its immediate vicinity and the surface area of the platinum electrode. Details of the underlying principles have been well described by Clark and associates\(^7\) and its clinical application has been discussed by Hyman et al.\(^7,8\) Although Vogel and co-workers\(^8\) have pointed out its usefulness in eight patients with small left-to-right interventricular shunts, the danger of explosion inherent in the handling of hydrogen and the hazard of an intracardiac electrode\(^9\) may have precluded its general acceptance thus far. Since no detailed evaluation of the use of this system in other conditions has appeared in the literature, 210 observations carried out in 60 patients with congenital heart disease are presented. This study emphasizes its present place in a diagnostic cardiac catheterization laboratory and gives examples of typical diagnostic tracings as well as of commonly encountered artifacts.

Material and Methods

During routine cardiac catheterization 210 observations were made in 60 patients with varying types of congenital heart disease. All procedures were carried out at the Cardiopulmonary Laboratory of the Children's Hospital Medical Center, Boston (table 1).

Although hydrogen inhalation for the detection of left-to-right shunts was more frequently applied in cases in which oxygen saturation data were considered equivocal in this regard, in general, the patients were unselected and were representative of a cross-section of our patients with congenital heart disease. They were all studied in the fasting, unanaesthetized state with only mild premedication consisting of meperidine, promethazine, and chlorpromazine.

Some of the infants and small children were asleep during the period of hydrogen inhalation. Most cooperated readily during the procedure. Ages ranged from 6 days to 29 years. There were only three patients over 18 years of age.

Analysis of blood samples for oxygen saturation was carried out by the standard spectrophotometric method with use of a Beckman type-B apparatus. Dye-dilution curves after injection of indocyanine green were sampled by a Colson cuvette and recorded on a Sanborn 550M 8-channel indirect photographic recorder through a 350-1600 pre-
amplifier. External electrocardiograms were available in all cases. Cardiac output was determined by the Fick principle in all, and, in addition, by dye-dilution technic in some of the children without shunts.

Arrival time is defined as the time lapsed from inhalation of the gas to the initial deflection of the baseline of the voltage from the intracardiac electrode.

Hydrogen appearance times on the venous side were detected in older children by commercially available platinum-tipped 5F or 6F Lehman electrode catheters, and in small infants by a 4F Lehman catheter, which had a bead of platinum cemented to its tip and the conducting wire contained within its lumen. Detection at the arterial sites was carried out by a 6-inch no.-23 platinum wire inserted either through an intra-arterial no.-20 needle or placed directly into the arterial lumen.

The electrode catheter or platinum wire was connected to a junction box by a length of no.-28 Teflon-covered wire, which was electrically shielded and could be sterilized. A second shielded cable led from a silver electrode on the patient's arm to the same box. Both the platinum and the silver electrode wires were directly connected through a junction box to the double-ended input of the electrocardiographic preamplifier, which was generally used with a sensitivity of 1/4 to 1 em./mv. (Fig. 1). In view of the high amplification needed, the intracardiac electrocardiogram was superimposed on all tracings recorded with the platinum-tipped catheter. This proved to be an advantage, for not only did the electrocardiogram serve as an indicator of the electrical continuity but also as a precise index of the catheter position as well.

Compressed hydrogen gas was transferred from a 10-L tank through a reducing valve into a 1.5-L rebreathing bag. The distal end of the latter was connected to a Statham strain-gage, type P23Db, to record the decompression of the bag upon delivery of the gas to the patient's airway. Arrival of the gas at the airway was timed by a thermistor placed at the nasal opening, which recorded the onset of inspiration. By observation of the thermistor curve on a monitor it was possible to release the hydrogen at early inspiration. The sudden cooling of the thermistor by the released hydrogen established the exact moment of entry of the gas. Generally, both signals were recorded simultaneously with the curve obtained from the

Table 1

<table>
<thead>
<tr>
<th>Means by which Diagnosis Was Established</th>
<th>H2 Electrode and O2 saturations</th>
<th>H2 Electrode and cine, dye, catheter position</th>
<th>H2 Electrode alone</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases with left-to-right shunt</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventricular septal defect</td>
<td>18</td>
<td>4</td>
<td>6</td>
<td>28</td>
</tr>
<tr>
<td>Atrial septal defect</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Patent ductus arteriosus</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Coronary arterioventricular fistula</td>
<td>1</td>
<td>1</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Anomalous pulmonary venous drainage</td>
<td>1</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Cases without left-to-right shunt</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic regurgitation</td>
<td>3</td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Pulmonic stenosis</td>
<td>0</td>
<td></td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>Normal</td>
<td>5</td>
<td></td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>5</td>
<td></td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Total no. patients</td>
<td>46</td>
<td>5</td>
<td>9</td>
<td>60</td>
</tr>
</tbody>
</table>

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hydrogen-detecting system. Near superimposition of both signals was required before a curve was termed acceptable. The proximal end of the gas-filled balloon was held above the patient's mouth and nose; a large clamp closed off the connecting tube to a standard face-mask. No attempt was made to determine the exact volume of gas delivered. In infants, care was taken neither to deliver too large a volume (average 600 ml.) nor to deliver it too close to the patient's face. In older children cooperation was readily obtained, and voluntary inhalation of the gas from a mouth-tube proved possible; this guaranteed delivery of larger volumes of gas. Since the time required for the passage of the inhaled hydrogen gas from the upper airway to the pulmonary alveoli is negligible, it has been included in the total appearance time.

Utmost care was taken to avoid all types of electrical sparks during the transfer of the compressed gas to the balloon, and to allow for sufficient time after inhalation to permit dispersal of the hydrogen. Meticulous attention to this part of the procedure is mandatory as a concentration of more than 5 per cent hydrogen gas in air has proved to be explosive.

No complications were noted in multiple administrations of hydrogen; the procedure was performed up to 10 times in several instances.

Proper sensitivity of the catheter tip could be verified in all but two cases, either by the detection of an early shunt curve, a recirculation curve, or by placing the catheter in the pulmonary vein or left atrium, and recording a normal early appearance time of less than a second. The two instances not showing these controls were called false negatives.

Although, initially, platinum black was used to increase the sensitivity of detection, repeated "poisoning" of the electrode, presumably by fibrin coating, led to the use of bare platinum metal. Even the bare platinum surface occasionally became "poisoned" and required cleaning with steel wool. Recently a double-ring tip has been used, whereby the external reference electrodes are obviated.

Results

Following the inhalation of hydrogen gas by the sedated but conscious patient, its arrival in a pulmonary vein or in the left atrium was detected in 0.6 to 1.2 seconds. In light of this early appearance time of the dissolved hydrogen gas in the left side of the heart, it was expected that only a slightly longer arrival time would be recorded at the site of emergence of a left-to-right shunt. In figures 2 and 3 are shown the appearance times in the venous side of the heart from

![Figure 2](http://circ.ahajournals.org/content/XXVIII/4/544.full)

**Figure 2**

**Arrival time of hydrogen gas in seconds in 210 measurements in 60 patients with and without left-to-right shunts. The mean arrival time in patients with shunt was 2.1 seconds (S.D. 0.9) and for patients without shunts 7.2 seconds (S.D. 1.9).**

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multiple determinations in 32 patients, in whom left-to-right shunts had been proved by one or more of the previously described methods (table 1). Also shown are the arrival times in patients in whom the presence of a left-to-right shunt was disproved. Four seconds form a reasonable, although arbitrary, line of separation between patients with and without left-to-right shunting. The five early appearance times recorded in three patients in whom a shunt could not be proved by other means were related to a high output state with rapid circulation time in two. These cases are discussed below.

The values of 1 to 4 seconds represent a wider range for shunt appearance times than has previously been reported.7-9 Because arrival time in seconds does not take into account variations in heart rate, appearance time was calculated in beats. By this method the degree of overlap is slightly greater (5.1 per cent instead of 3.8 per cent). Since there seems to be little advantage in this correction, the appearance time expressed in seconds is now routinely used.

The absolute arrival time in seconds did not permit identification of the exact site of left-to-right shunts. Very early appearance times occurred in patent ductus as well as in atrial septal defects. There was no difference in the average arrival time in the three major groups studied (fig. 3B).

A further observation common to all three methods of calculation is that the arrival time at the shunt and control sites seems to be independent of the size of the patient, at least in the pediatric age group (fig. 2).

There were 21 determinations in nine patients in whom no other corroborative laboratory evidence for left-to-right shunts or "high output" state was available (figs. 2 and 4 to 7). Since the appearance times in this group fell exactly within the distribution of early arrival times obtained in patients in whom the presence and site of left-to-right shunting was indubitable, this was considered sufficient proof and sole evidence of left-to-right shunting. The usefulness of the hydrogen indicator in these nine cases is beyond doubt.

Discussion

At present the hydrogen indicator technic is of greatest value in the following situations:

1. As an initial screening device for the detection and localization of small left-to-right shunts, usually showing flow rates of less than 2:1. In such instances the electrode catheter is placed in the pulmonary artery and at least two curves are obtained following two separate hydrogen inhalations. If the arrival time is greater than 4 seconds, the curves are accepted as recirculation curves and therefore as evidence against left-to-right shunting at any point. If, on the other hand, arrival times of less than 4 seconds are obtained, left-to-right shunting may safely be assumed; the level of the shunt is subsequent-

Figure 3
A. Significance of exact location of catheter tip. Additional observations in five cases with proved ventricular septal defect show a normal arrival time with the catheter tip low in the right ventricle. B. Arrival times of hydrogen gas in atrial septal defect, ventricular septal defect, and patent ductus arteriosus varied widely between 0.4 and 4.0 seconds.
ly localized by systemically recording curves from sites between the pulmonary artery and superior vena cava until a recirculation curve with arrival time greater than 4 seconds is obtained. Although the shunt can thus be localized to the most proximal chamber from which an early arrival time was recorded, the actual magnitude of the deflection and the actual arrival time in seconds are of little value in localizing the shunt because of the unpredictability of the effects of streaming within a chamber.

2. Hydrogen has also been very valuable in clarifying the diagnosis when oxygen saturation data provided inconclusive evidence of left-to-right shunting (figs. 4 to 7). In this respect, the recording of an early appearance time from the appropriate chamber enhances the value of equivocal oxygen saturation data. Similarly, the problem posed by the isolated highly saturated superior vena cava sample or by varying levels of saturation in the right atrium where hepatic and renal venous streams meet, may readily be solved by identifying anomalous pulmonary venous drainage, if present. Although theoretically coronary venous blood carries hydrogen gas, an early arrival time through this pathway has only been recorded in the two instances in which the catheter was placed in or near the coronary sinus (fig. 8).

3. During the course of any routine study, hydrogen may be of additional value in suggesting the presence of mild forms of valvular regurgitation by recording an early appearance time in a chamber proximal to the

Figure 4

Example of small patent ductus arteriosus in a 4-year-old boy. A continuous murmur was present but the oxygen data were inconclusive. Early appearances are noted in the pulmonary arteries, but not in the right ventricle. The thermistor curves in these and the following figures (at the top) rise with expiration, fall with inspiration, and move sharply down when the gas is delivered. This and the pressure drop in the bag are indicated by the first arrow, and arrival of hydrogen at the platinum is marked by the second arrow.
site of left-to-right shunting, when the latter is conclusively localized by oxygen data and other means to that chamber alone. For example, in patients with patent ductus arteriosus, pulmonary regurgitation was suggested by early hydrogen appearance in the right ventricle and was confirmed by angiocardiography. Similarly, tricuspid regurgitation associated with ventricular septal defect may be distinguished from an associated atrial septal defect by the use of a catheter with a second platinum ring placed 5 cm. proximal from the distal electrode.\(^{11}\) In these instances the arrival time of the hydrogen acts as an extremely sensitive indicator, which, while not diagnostic in itself, can be used in conjunction with angiographic and dye-dilution technics.

**Artifacts and Errors**

Utmost care must be taken to verify the proper responsiveness of the detecting catheter tip, since serious errors in interpretation may result otherwise (fig. 9). Two such instances were encountered that were not included in this series. One was the case of an 11-year-old girl with a known coronary AV aneurysm draining into an unknown site. Although initial hydrogen curves were negative, dye-dilution technics pointed to the right ventricular outflow tract as the site of drainage. It was then realized that the hydrogen procedure had failed because of unresponsiveness of the system. More recently the recommended verification procedures have been strictly followed and no such negative curves have been obtained.

In five patients with ventricular septal defect, late hydrogen arrival times were detected low in the body of the right ventricle, while a higher position of the same catheter tip permitted the recording of early arrival times (figs. 3 and 5). These records emphasize that errors in interpretation may arise if the position of the recording electrode is not carefully noted.

Three observations were made of early arrival of indicator in the pulmonary artery and right ventricle in a 13-year-old boy with severe aortic regurgitation (fig. 2). At surgery, aortic regurgitation was repaired by replacement of one of the posterior cusps but no ventricular septal defect was detected. Although it is well recognized that the ven-

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**Figure 5**

*Illustration of small ventricular septal defect in a 10-year-old patient not diagnosed by oxygen saturations, but confirmed by angiocardiography. The control time of systemic circulation is shown in the lower panel.*

**Figure 6**

*Records obtained in a 13-year-old patient with a small atrial septal defect. High superior vena cavael oxygen saturation was 80 per cent; right atrial, 82 per cent; right ventricular, 86 per cent; and pulmonary arterial, 85 per cent.*
A small ventricular septal defect was diagnosed in a 2-year-old girl by the early arrival time of hydrogen gas in the right ventricle. The wedge pulmonary venous appearance time (A) did not serve as a good control because no flow occurred along its tip. The small early curves in the right atrium and superior vena cava (E, F) may reflect coronary flow.

Several common artifacts have been observed (fig. 9). Shifts in baseline position can simulate an appearance curve. Figure 7E suggests a hydrogen arrival curve, although no hydrogen was given at that time. These spontaneous changes in baseline position can be differentiated from actual curves by the rapid return to the previous baseline level (figs. 7F and 9F). A true curve will usually require about 15 seconds to return to the baseline, since it takes this time for the hydrogen to wash out from the vicinity of the

tricular septal defect combined with aortic regurgitation may be small and difficult to locate, this case must be classified as our only instance of false positivity. One early curve, registered in each of two patients without shunt, not included in this study, with a consistent arrival time of 0.7 second in the femoral artery and of 1.7 second in the right side of the heart must be classified as a "high output" state. When a rapid circulation time inherent in the "high output" state is suspected, the limit of 4 seconds obviously does not apply. Presently, records are obtained simultaneously at the venous and arterial sides in all patients, so that these exceptional cases can be conclusively recognized.
electrode. The return of the curves to control baseline also depends on the amount of hydrogen inhaled and retained in the alveolar space. Other changes in baseline are caused by sudden changes in the position of the intravascular or reference electrode, or by the unusually deep respirations (fig. 9E). Also, rather commonly infants and young children when startled by the administration of a large volume of gas in a single "blast" may have baseline disturbances at the time of gas inhalation. Gentleness and care in the delivery of smaller volumes of hydrogen gas will eliminate this problem. Tight electrical connections are essential. Normal or slightly increased inspiration by itself will not alter the baseline (fig. 9C,D,E), except when the catheter tip is located in the right atrium.

Although the wedged pulmonary artery position has been recommended as a site to verify the appearance of the hydrogen gas in the pulmonary vascular tree, this was found to be unsatisfactory, since considerable differences were found in the arrival time (from 0.8 to 6.0 seconds) (figs. 7 and 8). Undoubtedly variations in position of the sensing element, differences in distance of the catheter tip from the alveolar membrane, and the possibility of interstitial obstruction to the diffusion of the gas make this procedure unreliable for verifying the responsiveness of the system. On the other hand, pulmonary venous sites, provided they are not wedged, invariably yield an accurate indication.

No untoward incidents have been encountered during these studies. Nevertheless, the

Figure 8
Arrival times in pulmonary artery (B) and right ventricle (C) via the ventricular left-to-right shunt in a 9-month-old child, are earlier than those of the gas diffusing back from the alveolar space to the wedged pulmonary artery catheter (A). When the catheter was positioned in the right atrium (D) or near the coronary sinus (E), a small early curve was registered, presumably representing coronary flow, but simulating a small left-to-right shunt via a patent foramen ovale or atrial septal defect. No such curve appeared on the control curve from the superior vena cava (F). All studies were done with the patient asleep.
Figure 9

Various types of artifact. Overzealous cooperation of an adult with a ventricular septal defect and pulmonary vascular obstruction (A, B) may result in involuntary breath-holding (Thermistor shows a flat line in the lower part of the tracing.) Increased but not excessively deep breathing by a 12-year-old boy with a ventricular septal defect yields higher curves than with normal respirations (C, D). Respiratory variation is rarely present except occasionally in the right atrial tracings (E). In a sleeping patient, a 2-month-old infant with cardiomegaly and cardiac failure with no shunt, the gas was delivered with excessive force (F); with normal force an equal appearance time results, although the curve is lower (G). Sudden shifts in baseline (also shown in figure 7E, F), are easily recognized by their short duration.

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highly explosive nature of hydrogen gas cannot be overemphasized. Adequate ventilation of the laboratory must be provided to prevent accumulation of the gas to concentrations approaching 5 per cent. Electrical equipment must not be switched on or off after the release of the gas until sufficient time has elapsed to permit adequate dispersion of the gas.

Furthermore, the hazard of inducing ventricular fibrillation and other arrhythmias via the internal electrode must be emphasized, since currents as low as 0.00004 ampere and 0.06 volt have been shown to induce ventricular fibrillation in dogs. The electrical equipment must be tested to insure that it will not induce such hazards. Careful attention to the connection of all electrical equipment to a common ground should be made.

Summary

In 60 patients with congenital heart disease 210 observations with hydrogen gas as an indicator for left-to-right shunts were recorded at cardiac catheterization. All but nine had other definite evidence of the presence or absence of left-to-right shunting. In these nine, 21 early hydrogen arrival times formed the only conclusive evidence of left-to-right shunting.

Although hydrogen and oxygen may form a highly explosive mixture, pure hydrogen used with proper precautions is a safe, reliable, and extremely simple indicator, eminently suited as a rapid screening procedure or as a supplementary tool in cases in which left-to-right shunts are difficult to prove.

Addendum

Since the completion of this report an additional 183 hydrogen curves, obtained from 26 patients, were analyzed, and the findings confirmed the conclusions reached above. There were 18 patients of the new total of 86 in whom oxygen data for a left-to-right shunt were equivocal; confirmation of the hydrogen results was obtained in 11 by means of surgery, cineangiocardiography, dye-dilution curves, and internal phonocardiograms.

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References


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