The Freon Test

A New Sensitive Technic for the Detection of Small Cardiac Shunts

By Kurt Amplatz, M.D., Robert F. Jeffery, M.D., Fredarick L. Gobel, M.D., Yang Wang, M.D., Gary E. Gathman, M.D., James H. Moller, M.D., and Russell V. Lucas, M.D.

SUMMARY
A new, sensitive, qualitative technic is described for detecting small left-to-right and right-to-left circulatory shunts. Advantages over other sensitive shunt detection devices are: (1) the use of a readily available, nonradioactive, nonexplosive, nontoxic gas, namely Freon 22; (2) the ability to sample through standard cardiac catheters as small as 5F; (3) an immediate answer due to recording of the gas concentration in blood; and (4) extremely high sensitivity allowing the detection of the smallest left-to-right and right-to-left shunts.

Additional Indexing Words:
Angiocardiography      Dye-dilution studies      Fluorinated hydrocarbon
Radioactive methyl iodide  Inhalation test       Oximetry

One of the difficult problems in cardiac catheterization is the identification and localization of small left-to-right shunts. This is particularly trying with small residual shunts following intracardiac surgery. It is recognized that standard oximetry, indicator-dilution curves with injection into the right heart, and right-sided angiocardiography are not sensitive enough to identify small left-to-right shunts. As a result, several very sensitive technics using radioactive gases such as methyl iodide, krypton, or xenon, have been developed. However, the handling of radioactive gases in an improperly ventilated catheterization laboratory is hazardous, and expensive and complex detection equipment is usually required. Furthermore, multiple blood samples may have to be drawn and counted individually. Hydrogen, although easily and elegantly detected without sampling, has the disadvantage of being a highly explosive gas, and its detection requires a special catheter. Nongaseous indicators may be used for detecting small shunts only if injected directly into the appropriate left heart chamber. This presents obvious difficulties when dealing with atrial septal defects. Furthermore, left heart catheterization may be relatively difficult and time consuming, especially in the young.

It is the purpose of this communication to describe a simple test for the detection of small cardiac shunts utilizing Freon* as an indicator and a commercially available halogen leak detector as the sensing device.† This method has the advantages of being

*Freon is the registered trademark of Dupont fluorinated hydrocarbons.
†General Electric type H2 leak detector.
easy to perform with standard cardiac catheters and safe for patient and operating personnel. Our experience with this method in 178 patients indicates its reliability in detecting even extremely small left-to-right shunts.

Although the halogen leak detector allows sensitive detection of all types of halogens, the fluorinated hydrocarbon compounds (Freons) appear to be particularly advantageous. The Freon compounds are stable, nonflammable, inert gases with an extremely low toxicity and are therefore widely used as propellants in spray cans and as refrigerants. Some of these Freons, for example C318, are tasteless, odorless compounds which have even been accepted by the United States Food and Drug Administration as food additives, particularly as propellants for dessert toppings. Experience has shown that the widely used, inexpensive Freon 22 is a very suitable indicator gas. The Freons are listed in the Underwriters' Laboratories as toxicity group 5 and 6, the least toxic agents known. A continuous exposure to an atmosphere of 20% of several listed Freons for two hours does not produce any demonstrable injury.

Basic Principle

The patient is given a single inhalation of Freon through a simple inhalation apparatus which will be described in detail below. The cardiac catheter is connected to the micro-roller pump A (fig. 1) which draws blood at a slow steady rate (0.2 cc/sec) into a plexiglass spray chamber B. To force the dissolved Freon from the bloodstream, the sampled blood is atomized by a small high velocity CO₂ jet, regulated by reducing valve C. The carbon dioxide and the removed Freon gas pass from spray chamber B into the sensing unit D which in turn is connected to the control unit E. According to the concentration of Freon in the blood, the signal is fed into the recorder F and plotted as a time concentration curve of Freon in the blood sample. This diagnostic unit is portable and can be freely moved about (fig. 2).

Equipment

There are four basic components for this study: (1) a method to deliver the Freon, (2) a method to withdraw blood from the catheter, (3) a Freon detector, and (4) a recorder (fig. 1).

Inhalation Apparatus

A 5,000-cc anesthesia rubber bag containing 5% Freon 22-air mixture is attached to a standard anesthesia mask by the three-way valve A (fig. 3). The air inlet is closed by depressing a ball valve, and the patient is connected to the Freon-air mixture contained in the rubber bag B (fig. 3). The patient is given a single inhalation. The almost odorless gas does not cause any objective or subjective physiologic changes. The exact time of inhalation is made audible by a built-in whistle which allows precise recording of the start of inhalation. This system has been successfully used in children and uncooperative patients.

The Sampling Device

A variable rate peristaltic micro-roller pump* allows the reliable slow withdrawal of blood in almost nonpulsatile fashion. Thick-walled vinyl tubing with small internal diameter (ID, 1/30 inch; OD, 5/30 inch) is used to assure constant strong negative pressure. Sampling time is measured for various catheters, using blood. The major factor determining catheter times in this system is length. The dead time in the machine is a constant 1.5 sec. Catheter times vary from 4 sec for an 80-cm 5F catheter to 9 sec for a 150-cm 8F catheter. All appearance

*Masterflex tubing pump with solid state speed control (Cole-Parmer, 7330 North Clark Street, Chicago, Illinois 60626).
times are subsequently corrected for the catheter used. A standard recording system for dye-dilution curves is very suitable for Freon studies.

The Halogen Leak Detector

The leak detector is a highly sensitive, commercially available instrument which is well known to air-conditioning and refrigeration servicemen. Basically, it consists of a cylindrical, heated platinum element over which the sample gas is drawn. If traces of any type of halogen gas are present (the halogen gases are bromine, fluorine, iodine, and chlorine and their compounds), ionization occurs in the interelectrode space and causes an increase in conductance which is proportional to the amount of halogen present. An electromagnetic signal is achieved which can be directly read out from the leak rate meter. The unit is designed to allow the reliable detection of minute halogen leaks in the order of $1 \times 10^{-8}$ standard atmospheric cc per second of Freon 12. This in turn corresponds to a leak rate of $6 \times 10^{-5}$ ounces per year. At this leak rate it would take approximately 270,000 years for 1 pound of refrigerant to completely evaporate! The sensitivity of the control unit can be adjusted by a 10-step selector switch. For the definitive detection of even the smallest cardiac shunts only the medium sensitivity range is used.

Left-to-Right Shunts

The first Freon inhalation study is carried out with the catheter tip in the pulmonary artery. If this study indicates a normal venous return pattern, all intracardiac left-to-right shunts at, and upstream to, the pulmonary artery level are excluded. If a shunt curve is recorded, further inhalation studies are performed at the ventricular or atrial levels to localize the exact site of the shunt. Since the inhaled indicator gas is rapidly cleared through the lungs, several studies can be done in rapid succession without much background interference.

As with other indicator technics, the normal return to the right heart is evidenced by a delayed appearance time (6 to 20 sec) and by a slow, gradual rise of concentration reaching a plateau after approximately 30 sec (fig. 4). Normal venous return curves tend to be low in
comparison with shunt curves due to diffusion of indicator gas into extravascular spaces in the peripheral capillary bed.

In the presence of a left-to-right shunt, however, indicator gas appears early and in large concentration in the blood sample causing a characteristic steep rise of the curve (fig. 5). Contrary to the gradual upswing and plateau of normal venous return, the shunt curve usually peaks relatively sharply. The main differentiating features of the shunt curve from the normal venous return curve are therefore: (1) short appearance time as compared with that obtained upstream to the shunt (most important), (2) steep, sharp rise, and (3) increased height even in minute left-to-right shunts. In order to make the appearance time clearly visible, the sensitivity is increased to such an extent that the curves go off the paper and the diagnosis is therefore based only on appearance time and abruptness of rise.

Right-to-Left Shunts

The apparatus can also be used for sensitive detection of right-to-left shunts by using Freon dissolved in saline. Although Freon 22 can be used, Freon 21 is preferred because of its higher solubility. Three cubic centimeters of Freon 21 are withdrawn into a syringe containing 5 cc of saline, and the gas is dissolved under manual pressure. This solution is injected through a catheter into the right side of the heart and blood is sampled continuously from a peripheral artery. Early appearance time indicates the presence of a right-to-left shunt. This technic represents a highly sensitive, inexpensive screening procedure for the presence of right-to-left shunts but for quantification it cannot take the place of dye-dilution curves.

Results in 178 Cases

Freon inhalation studies were performed in 178 patients during cardiac catheterization. The patients ranged in age from 4 to 68 years. No complications were associated with the Freon inhalation study. The presence or absence of a cardiac left-to-right shunt was also documented by standard oximetry technic, dye-dilution curves, blood-oxygen determination, radioactive methyl iodide inhalation, or selective angiocardiography. Not every patient had all of the listed tests, but at least one method of shunt detection other than the Freon test was carried out.

The results of the various studies are summarized in table 1. In 176 of the 178 patients studied with the Freon inhalation test, the results were in agreement with the clinical and other laboratory features. In all of the 115 patients without left-to-right shunts, the Freon inhalation study revealed a normal venous return.

Of the 62 cases in which the Freon test indicated a left-to-right shunt, 12 could not

---

**Table 1**

<table>
<thead>
<tr>
<th>Freon</th>
<th>Result</th>
<th>Oximetry</th>
<th>Methyl Iodide</th>
<th>Angiography</th>
<th>Dye</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Pos.</td>
<td>37</td>
<td>8</td>
<td>29</td>
<td>31</td>
</tr>
<tr>
<td>62 patients</td>
<td>Neg.</td>
<td>25</td>
<td>0</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Negative</td>
<td>Pos.</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>116 patients</td>
<td>Neg.</td>
<td>86</td>
<td>19</td>
<td>38</td>
<td>79</td>
</tr>
</tbody>
</table>

* Some patients had more than one additional study.

Circulation, Volume XXXIX, April 1969
FREON TEST

be confirmed by oximetry, dye curves, or selective right-sided angiography. However, none of these 12 had left-sided catheterization. Three of these 12 patients had clinical evidence for a small ventricular septal defect, namely, a characteristic systolic murmur. Eight others had recatheterizations performed 1 year following surgical repair of ventricular or atrial septal defects. The remaining patient, a 14-year-old boy, had had surgical correction for valvular pulmonary stenosis 1 year previously. At pre-surgical catheterization the Freon study from the pulmonary artery had been negative for shunt. At postoperative catheterization, the corrected appearance time was 2 sec in the pulmonary artery and 9 sec in the right ventricle. There was no other clinical or laboratory evidence of left-to-right shunt. However, a murmur of pulmonary insufficiency was present, and we suspect this case represents diastolic backflow of blood from pulmonary capillaries to main pulmonary artery.*

Both the methyl iodide test and selective left-sided angiography agreed with the Freon test in all cases in which both examinations were performed. Sometimes, however, the shunt was so small that it was seen with difficulty on selective angiography.

Only one false negative Freon test was found. This failure was due to faulty sampling through an end-hole catheter. These sampling difficulties are extremely rare if samples are obtained from the pulmonary artery or right atrium but rather common with ventricular sampling. In the right ventricle a catheter may be partially occluded by muscle, especially during systole, with resultant nonsteady flow. Whenever possible, therefore, the first sample should be drawn with the catheter freely moveable in the pulmonary artery which usually allows the diagnosis or exclusion of a left-to-right shunt.

In one case, a false positive Freon test was produced by sampling through a catheter which was wedged in the pulmonary artery. Following withdrawal of the catheter to the main pulmonary artery, however, the test was negative.

In 10 cases, right-to-left indicator-dilution curves were obtained using Freon 11 dissolved in saline. Sampling and injection sites were identical to concurrent dye-dilution curves. There was uniform agreement between the results obtained on use of Freon and indocyanine green.

Discussion

Since Freon compounds are so widely used in various sprays, fire extinguishers, air-conditioning units and, particularly, household refrigerators, industry has developed very sensitive devices for detecting minute leaks in such systems. It appeared logical to use such a sensitive halogen leak detector for the demonstration of small cardiac shunts. The constant withdrawal of a very small blood sample through standard cardiac catheters by means of a roller pump, and spray vaporization of previously inhaled Freon from blood with an inert gas stream is a comparatively simple and foolproof technic. The answer is immediately obtained. The use of special electrode catheters, precautions against explosions, or protection of operating personnel against radioactivity are superfluous. Since the technic is based on the indicator-dilution principle, the curves obtained allow a definite diagnosis although the size of the shunt cannot be exactly calculated. Large shunts are readily diagnosable by standard oximetry. Cardiac left-to-right shunts demonstrable only with a Freon test are usually of the order of 20% or less. Quantification of Freon concentration is feasible as far as the leak detector is concerned. The extraction of Freon from the blood sample, however, by means of a CO₂ jet is incomplete and may well vary with the

*Since presentation for publication we have had another similar case, a young boy with pulmonic insufficiency. Corrected Freon appearance time was 1 sec in the pulmonary artery and 2 sec in the right ventricle. There was no corroborative evidence of left-to-right shunting.

Circulation, Volume XXXIX, April 1969
amount of gas dissolved. Furthermore, the amount of Freon delivered to the pulmonary capillary blood is difficult to control. Therefore, no attempt has been made to make this test quantitative. The described technic has the advantage of using standard catheters as small as no. 5 French and a nonradioactive nonexplosive gas. The main advantage of the technic is believed to be its unsurpassed sensitivity.

Spontaneous Closure of a Ventricular Septal Defect

Certain features of congenital heart disease at once command attention. In the first place there is a fixed anatomical lesion with structural alterations in the heart that cannot be removed. Consequently the course of the patient is largely moulded by the factor of adaptation, and the interplay of various mechanical forces in order to assure an adequate circulation despite the handicap of a gross anatomical abnormality. Exceptionally, some lesion such as an isolated interventricular septal defect, which may be of considerable importance when the heart is small, may become, as the heart enlarges with normal growth, unimportant relative to the size of the heart as a whole, and its physical signs may disappear.—JAMES W. BROWN: Congenital Heart Disease. London, John Bale Medical Publications Ltd., 1939, p. 1.
The Freon Test: A New Sensitive Technic for the Detection of Small Cardiac Shunts

KURT AMPLATZ, ROBERT F. JEFFERY, FREDARICK L. GOBEL, YANG WANG, GARY E. GATHMAN, JAMES H. MOLLER and RUSSELL V. LUCAS

_Circulation._ 1969;39:551-556
doi: 10.1161/01.CIR.39.4.551

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1969 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/39/4/551

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at: http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at: http://circ.ahajournals.org//subscriptions/