Measurement of Circulation Times with NaI$^{131}$

By Réginald A. Shipley, M.D., and Richard E. Clark, B.S.

Circulation time from an arm vein to the femoral artery as determined with I$^{131}$ averaged 11.2 seconds in normal male adults. In the presence of heart failure the time of initial arrival was prolonged, and the slope of ensuing rise flattened. Decholin time, determined simultaneously, averaged 25 per cent longer than I$^{131}$ time in both normal subjects and patients with congestive failure. Theoretical considerations indicate that arrival time measured with a radioactive tracer is less affected by cardiac dilatation than is arm to tongue time obtained with Decholin. Arm to heart time measured with I$^{131}$ was prolonged in the presence of failure but marked overlap with normal subjects was evident.

Little attention has been given to the determination of simple circulation time with a radioactive tracer since the classical studies of Blumgart and Weiss nearly 30 years ago. The apparatus employed by Blumgart and Weiss consisted of a shielded, air filled, detection chamber in which ionization was induced by gamma radiation from blood-borne radium-C. Activity was recorded by a pen galvanometer connected to a vacuum-tube amplifier. Although the technical aspects of their procedure were formidable, circulation time can now easily be measured with a scintillation counter and a suitable gamma emitting radioisotope. In clinical application a radioactive test substance has the virtue of providing a completely objective endpoint. Moreover, the injection of such a substance is not attended by any unpleasant side effects.

Although the equipment employed by Blumgart and Weiss might have recorded the earliest time of arrival with a fair degree of accuracy, a curve corresponding to the expected rise in concentration between the arrival of first traces of material and the attainment of a peak was not delineated. Present recording devices allow visualization of the entire time-concentration curve at the site of measurement. Because the upslope of such a curve has physiological significance, the present study includes measurements of rise-time, in addition to the time of earliest arrival.

From the Radioisotope Service, Veterans Administration Hospital; the Department of Medicine, Western Reserve University, Cleveland, Ohio.

Received for publication February 29, 1956.

Methods and Subjects

Ninety-one male subjects from the medical wards of the hospital were included in the study. The normal group numbered 50 and included individuals between the ages of 20 and 69 (median 37) who were not seriously ill, and who were suffering from no cardiac disorder or other diseases such as hypertension, severe emphysema, hyperthyroidism or anemia, which could either lead insidiously to heart failure or directly affect the rate of circulation. There were 16 cardiac patients in whom decompensation was considered to be severe or moderate, and 9 in whom it was judged to be mild. The remaining patients who were not completely normal by the aforementioned standards were used only for a comparison of the I$^{131}$ arm to femoral time with the conventional arm to tongue time obtained by a simultaneous injection of Decholin.

Tests were performed in the recumbent position with the arm resting horizontally at the side. The test material consisted of 15 to 50 μc of NaI$^{131}$ contained in 3 ml. of 20 per cent Decholin injected into a cubital vein of the right arm. With a 20 gage needle it was nearly always possible to complete the injection within less than 2.5 seconds. The median duration was 1.8 seconds. More rapid delivery was not attempted because of the intent to duplicate the routine technique employed in the clinical determination of circulation time. The beginning of injection was the reference point of measurement for all time intervals.

A shielded scintillation counter collimated by a circular opening 1/4 inches in diameter and 1/4 inches long was placed over the femoral artery at the groin. A second counter with a collimator 1 inch in diameter and 1/4 inches long was placed over the sternum in the region between the 2nd and 4th ribs slightly to the right of the mid line. Radioactivity was recorded by means of an Esterline-Angus graphic ammeter connected to a rate meter having a time constant of 0.5 second.
RESULTS AND DISCUSSION

Arm to Femoral Time. The mean time from the beginning of injection until the arrival of activity over the femoral artery in the series of normal subjects was 11.2 seconds (table 1, fig. 1). This is very close to the mean arm to hand time obtained with radio-sodium in young children by Hubbard and co-workers, but considerably shorter than that of Blumgart and Weiss whose mean normal arm to arm time was 18 seconds. The mean arm to femoral time for severely decompensated cardia was prolonged to 35.1 seconds. The length of time required for the activity to reach a maximum after its first arrival averaged 8.0 seconds in normal subjects as compared to 25.1 seconds for the cardiac patients.

Comparison of Arm to Femoral and Arm to Tongue Time. The expected correlation between arm to femoral time and Decholin time is shown graphically in figure 2. It is readily apparent that femoral time was shorter than arm to tongue time in all instances save two. The difference was usually 2 to 4 seconds in noncardiacs, but it averaged 8 seconds in the decompensated patients (table 1). Expressed another way, Decholin time exceeded arm to femoral time by approximately 25 per cent in the combined series.

The relative delay in the lingual endpoint as compared to the arrival of the first detectable activity at the femoral artery is not unexpected. Contributing to the delay are the time for lingual diffusion, and hesitation by the patient before signalling recognition. Perhaps most important is the fact that the rise in concentration of Decholin in the tongue, like that of radioactivity at the femoral artery, is more or less gradual, rather than abrupt (fig. 3). A lag is therefore to be expected between arrival of the first traces of Decholin and attainment of the threshold concentration required for the perception of a bitter taste. The greater prolongation of Decholin time than I\textsuperscript{131} femoral time in the presence of decompensation is undoubtedly related to the slower rise in concentration of test substance at the point of detection.

That decompensation is attended by a more

| Table 1.—Summary of Measured Time Intervals (seconds) |
|-----------------------------------|---|---|---|---|
| No. Cases | Mean | Median | Range |
| Arm-femoral* | Normal 50 | 11.2 | 10.8 | 5.5-18.5 |
| | Failure 16 | 35.1 | 33.8 | 10.0-67.0 |
| Rise time (Femoral) | Normal 49 | 8.0 | 7.5 | 4.0-17.0 |
| | Failure 16 | 25.1 | 22.5 | 11.0-51.0 |
| Decholin | Normal 50 | 14.4 | 14.0 | 8.5-24.0 |
| | Failure 14 | 43.1 | 42.3 | 19.5-78.0 |
| Arm-Heart* | Normal 48 | 1.8 | 1.5 | 0.8-5.0 |
| | Failure 15 | 4.3 | 4.0 | 0.8-11.0 |
| Arm-heart peak | Normal 48 | 7.0 | 6.5 | 3.0-16.5 |
| | Failure 14 | 19.9 | 17.8 | 6.0-44.0 |
| Rise time (Heart) | Normal 48 | 5.2 | 4.8 | 1.5-13.5 |
| | Failure 14 | 14.5 | 13.8 | 3.0-37.0 |

* Earliest arrival
† Failure considered moderate to severe
§ St. E. of Mean

![Fig. 1. Frequency distribution of values for arm to femoral time in normal and decompensated subjects.](http://circres.ahajournals.org/DownloadedFrom)
exponential discharge follows rapid mixing, it may be shown\(^6\) that the slope of rise in concentration of a test substance measured at a peripheral artery will be inversely correlated with the volume of the heart chamber. Because a more gradual slope will necessarily delay the attainment of the critical level for lingual perception of taste, cardiac dilatation alone may produce a prolonged Decholin time. A correlation with heart size has in fact not only been repeatedly observed,\(^6,9\) but the relationship of slope of rise to arm-to-tongue time recognized.\(^6,9\)

Another deduction based on the principle of rapid intracardiac mixing and exponential discharge is the lack of influence of heart capacity on the time of first arrival of test substance at a point beyond the heart. A delayed time of onset in rise would occur only in the presence of decreased volume flow (cardiac output) or an increased volume of blood in tubular channels outside the heart. The relationship would be expressed by Stewart's formula: \( t = q/F \), where \( t \) is time, \( q \) the volume of blood contained in the arteries and veins, and \( F \) the volume flow per unit time. Although it is likely that axial streaming is of sufficient magnitude to partially invalidate this formula, not only for the earliest time of arrival but even for mean time, the model is probably no less applicable in decompensated patients than in normal subjects. The delay in earliest arrival which attends failure may therefore result from varying combinations of reduction in cardiac output and increase in extracardiac blood volume.

**Arm to Heart Time.** Recorded in table 1 are the arrival times of the first detectable radioactivity over the heart, the timing of peak activity, and the length of rise between the two. It may be noted that although the mean value for time of arrival is lengthened in the presence of congestive failure, overlap with the normal group is wide, and intragroup variability is quite extensive. This was observed also by Blumgart and Weiss.\(^10\) The present study indicates that the time of attainment of peak activity is just as variable as arrival time.

In spite of an attempt to place the counter over the right atrial region, the recorded tracings invariably included a component which was ascribable to the left heart or its outflow...
tract (fig. 3C−F). In most normal subjects (fig. 3C), and in an occasional cardiac patient (fig. 3E), the right heart component could be visualized as a separate peak. In the remaining tracings the curve assumed the form of a single prolonged hump. Such a contour may be explained by the transit of a column of tracer which is so long as to be viewed simultaneously from structures comprising both the right and left side of the circulation. This distortion would be magnified by the slow rate of injection here employed, and would be expected most often in the presence of failure wherein clearance from the heart chambers is delayed because of dilatation. The summit of the broad single hump, although used in the tabulation for the timing of peak concentration, is not identical with that of the true right heart peak. The latter, if it were not obscured by the effect of summation, would appear earlier.

The mean time between injection and passage of tracer to the right heart can be calculated only by derivation of an entire pure right heart curve by extrapolation. Even if the first peak is clearly delineated tracings usually do not provide a sufficient length of subsequent downslope to permit such a calculation when, as in the present study, measures are not taken to propel the tracer rapidly into the heart.

**Summary**

The circulation time to the femoral artery as determined by the earliest arrival of $^{131}$I after injection into an arm vein averaged 11.2 seconds for 50 normal subjects. The range was 5.5 to 18.5 seconds. In the presence of heart failure the time tended to be longer than normal and the ensuing slope of rise in radioactivity decreased.

Decholin time exceeded arm to femoral time by an average of 25 per cent. A cause of the relatively flat slope of rise in concentration of the test substance, Decholin perception is delayed longer in decompensated patients than in normal subjects. Cardiac dilatation alone may flatten the slope and thereby increase Decholin time, but the earliest $^{131}$I time should not thereby be materially altered.

The time of transit of the first portion of radioactivity reaching the heart after injection into an arm vein averaged 1.8 seconds for normal subjects. Peak activity was attained at a mean time of 7.0 seconds. Although the corresponding mean values were higher in the presence of failure, an extensive overlap with the normal range was apparent for individual readings.

**SUMMARY IN INTERLINGUA**

Post injectar $^{131}$I in un vena del bracio, le tempore del circulation usque al arteria femoral esseva mesurate in 50 subjectos normal. Le intervallo median usque al arrivata del prime $^{131}$I esseva 11,2 secundas, con valores minimo-maximal de 5,5 e 18,5 secundas. In le presentia de disfallimento cardiac le intervallo monstравa un tendentia a exceder le normal, e le sequente ascendita de radioactivitate esseva reducute.

Le tempore decholinic excedeva le intervallo ab bracio a femore per un valor median de 25 pro cento. A causa del relativemente lente ascendentia del curva de concentration del substantia testatori, le perception de Decholina es plus retardate in patientes discompensate que in subjectos normal. Le dilatation cardiac per se pote applattar le curva e assi augmentar le tempore decholinic, sed isto non debera resultar in un alteration significative del, tempore del prime arrivata de $^{131}$I.

Le intervallo ab injectiones bracial usque al arrivata del prime radioactivitate al corde habeva in subjectos normal un valor median de 1,8 secundas. Le maximo de activitate esseva attingite post un intervallo median de 7,0 secundas. Ben que le valores correspondentie esseva plus alte in le presentia de disfallimento cardiac, le distribution del valores individual in le duo gruppos de individuos con e sin disfallimento monstравa un extense region de coincidentia.

**REFERENCES**


Editorial Responsibility

Practically every editorial that has appeared on this page has been criticized by one or more readers. . . . Most of the criticisms express a point of view different from that of the editorial writer. Such letters are always welcome, for, if the topic is worth discussing, it is healthy to examine alternative points of view.

A few criticisms are written to correct errors. . . . An occasional letter takes us to task on the ground that no editor should be so presumptuous as to think that he can speak for American scientists. Right; none does. This is the reason why all editorials are signed. . . . If he says anything of importance, fine; if he is provocative and stirs up a useful controversy, also fine; if he writes drivel or says something that is wrong, the error is his, not the Association’s and not science’s.  

(Signed) D. W.

Measurement of Circulation Times with NaI\textsuperscript{131}

REGINALD A. SHIPLEY and RICHARD E. CLARK

*Circ Res.* 1956;4:456-460
doi: 10.1161/01.RES.4.4.456

*Circulation Research* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1956 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/4/4/456

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Circulation Research* 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 Research* is online at:
http://circres.ahajournals.org/subscriptions/