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**Pharmacologic Dynamic Response Index**

Department of Medicine and Surgery

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NAVAL AIR DEVELOPMENT CENTER  
JOHNSVILLE  
WARMINSTER, PA. 18974

Aerospace Medical Research Department

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A Cardiovascular Dynamic Response Index

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Prepared by:

*Richard J. Crosbie*  
Richard J. Crosbie, M.A.

*Carl T. Reichwein*  
Carl T. Reichwein, B.S.E.E.

*Emma Fessenden*  
Emma Fessenden, M.S.

Released by:

*D. Morris*  
D. Morris, CAPT, MC, USN  
Director  
Aerospace Medical Research Department

## SUMMARY

Human tolerances to accelerating forces long have been recognized as being dependent on the magnitude, direction, and duration of a given G. Experimentally derived tolerance curves for positive G have been reported by Stoll and Kydd. The former provides the time (time at peak plus rise time) at which a given end-point (PLL) will occur for various sustained G levels while the latter provides the period of a haversine shaped G profile which will produce the same end-point for various peak G's. Aerodynamically derived G profiles take on a wide variety of shapes and forms. Any attempt at predicting human tolerances to such profiles from either of the above tolerance curves directly would be extremely difficult if not impossible. Using a lumped parameter description for both the arterial and venous portions of the cardiovascular system, a simplified mathematical model has been derived which includes a feedback loop for changes in cardiac output and peripheral vascular resistance to represent the non-linear effects of cardiovascular reflexes. The model, which describes the transient and steady state response of the system to any shaped G profile, has been programmed on an analog computer. By identifying a particular response of the system to correspond with a given end-point (PLL), a cardiovascular dynamic response index (CDRI) has been defined. By using the CDRI, the model provides agreement with both the Stoll and Kydd tolerance curves. The model may further be used in predicting human tolerances to such a variety of G stress conditions as the following: (1) varying shaped G profiles where the effect on the cardiovascular system is the primary concern; (2) extremely high positive accelerations for short durations where controlled experiments are either impossible or too hazardous to perform; (3) variations in the degree of supination which the subject assumes for a given G profile.

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## INTRODUCTION

Human tolerances to accelerating forces have long been recognized as being dependent on the magnitude, duration, and direction of the G force on the individual. Existing G time-tolerance curves (experimentally derived) differ depending on the definition of the tolerance limit and the shape of the forcing function used.

Human tolerance is associated with a physiological end-point and those most commonly used are grayout or peripheral lights lost (PLL), blackout or center lights lost (CLL), and unconsciousness. Even within these tolerance definitions there exists a range of variability depending, among other things, on the duration of the end-point. Leverett and Zuidema (1) have cautioned that if PLL or CLL is used as an end-point, then agreement should be reached as to how long loss of vision is to last. Various authors have defined G duration to be the time at maximum G (2), the time from G onset to the end-point occurrence (3), or the total time of the G profile (4).

The application of controlled experimental data to the analysis of realistic combat mission G-profiles is made difficult not only because of the variability in the definition of tolerance limits but as is often the case, the complex shapes of the combat mission profiles cannot be directly related to the simplified experimental profiles. On practical grounds, empirical tolerance curves for every possible shape of combat mission G-profiles cannot be generated or documented using past laboratory techniques.

## APPROACH

Fundamentally, a subject's end-point is indicative of the inertial reaction of his body, in particular his circulatory system, to the dynamic forces imparted to it during the G-profile. When viewed systematically, the circulatory response to acceleration is completely dependent on the response mechanism itself and the time history of the acceleration input. It is apparent then that documenting stimulus-response pairs becomes an insurmountable task when a complete definition of tolerance limits for all possible G-profiles is sought.

To achieve the goal of being able to predict human tolerability to arbitrary G-profiles, an approach has been developed which differs substantially with the stimulus-response tabulation technique. This new approach requires a quantitative description of the mechanism which produces the tolerance end-point and its dynamic response to an acceleration input. In support of this requirement a computer model of the acceleration response mechanism has been developed which provides a functional description of those physiological processes directly related to the end-point symptoms during and after the application of a G stress. It is not intended for the model to accurately provide a detailed manner in which these processes take place; its main purpose is to faithfully reproduce the effect of these processes on the presence and duration of an end-point as a function of the G-profile presented.

Using the model, the empirical tolerance curves produced over the past years can be consistently duplicated even to the point of showing how the different definitions of end-point and G-duration can account for the discrepancies among the experimental curves.

#### METHOD

Since the G tolerance we are concerned with here is expressed in terms of the visual symptoms of grayout and blackout, the general strategy of developing the computer model was based on the physiological mechanism producing such symptoms. Duane (5) observed that, under acceleration, the symptoms of grayout and blackout were correlated with the cessation of blood flow in the retina. Coupling this with the fact that, under conditions of constant vascular tone, flow is directly proportional to the vascular resistance, the basic scheme of the model took shape.

The first item was the generation of representative mean arterial and venous pressures at the head level. This was done by adjusting computer parameters until the computed pressure curves matched those recorded in acceleration experiments by Henry et al. (6) and shown in Figure 1. Each curve was composed of two components: the hydrostatically induced pressure drop which slightly lags the acceleration profile and the delayed compensatory increase in pressure initiated mainly by the carotid sinus baroreceptors.

The block diagram of the computer model is shown in Figure 2. The G-profile is fed directly into the arterial and venous systems to produce the hydrostatic responses of each system. The mean arterial pressure is fed into a model of the carotid reflex mechanism which detects any pressure deviation from the resting pressure (80 mm Hg.). The output of the reflex system is used to control the venous pressure by controlling the stiffness or tone of the venous model and to control the arterial pressure by controlling the set point (aortic pressure (7)) directly and indirectly by controlling the tone of the arterial model. The parameters and time constants of both the arterial and venous system as well as the reflex mechanism were adjusted to produce results comparable to those obtained experimentally (Figure 1).

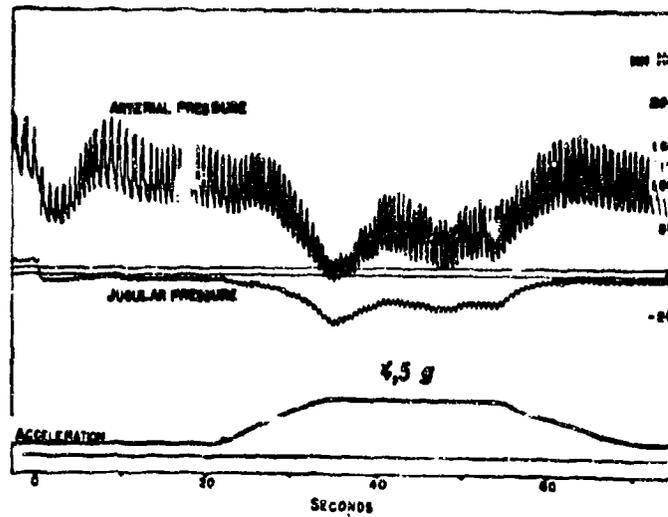


Figure 1. Arterial pressure at head level and pressure in the jugular venous bulb. (Henry, 1956)

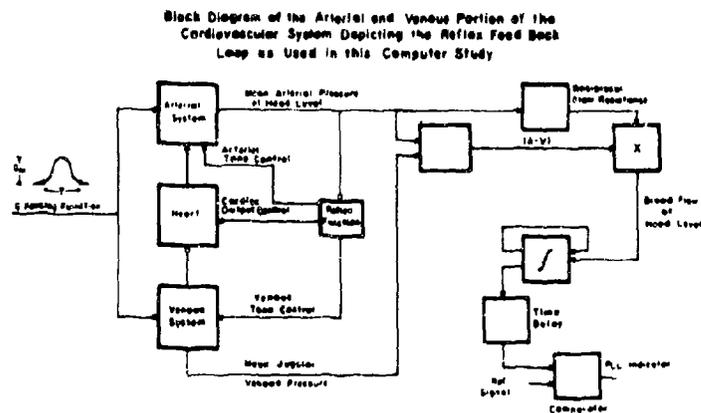


Figure 2. Block diagram of the mean arterial and venous portion of the cardiovascular system depicting the reflex feedback loop as used in this computer study.

A non-dimensional quantity equivalent functionally to retinal blood flow was formed from the arterial and venous pressures by multiplying the arterio-venous difference by the reciprocal of vascular resistance which, in the range of low pressures involved here, is nearly proportional to the arterial pressure itself. In this respect, the minimum value of the arterial pressure was limited to 0 mm Hg. while venous pressure was permitted to fall as low as -60 mm Hg. The net effect of all of this was that flow functionally followed the arterial pressure at low arterial pressures (0-40 mm Hg.) and the A-V difference at higher pressures (60-100 mm Hg.).

The hypothetical blood flow parameter was fed into a first order lag circuit and time delay to represent possibly the decay of the retinal oxygen supply to some threshold level at which point grayout can be said to occur. This corresponds to the experimental observations made by Duane(5) on the time delay between retinal exsanguination and the onset of grayout and blackout.

In the computer model a comparator was used to indicate the point at which the retinal oxygen supply fell below a preset threshold value. It was found, during the development of the model, that a single threshold value could be used to reproduce the tolerance curves found experimentally. This value has thus been termed a cardiovascular dynamic response index (CDRI).

## RESULTS

As an initial test of the CDRI model, it was applied to results reported by Kydd (4) in which a haversine shaped G-profile was used as a standard stimulus to obtain human tolerance data. This data relates the period at the haversine curve with the peak G value which will produce a PLL end-point. In these experiments the peak G was routinely increased by small steps for each haversine period until the subject gave indication of PLL for a period of about 2 seconds. Since the runs were generally on the downward slope at this time, the haversine G profile was normally continued with the subject indicating the time at which peripheral lights returned. A television camera was used to monitor the subject to insure he did not turn his head to either side during a run. In these experiments the total shape of the G-profile including both the rise and fall portions are assumed to contribute to the final result.

Having already adjusted the necessary parameters of the computer model to bring about agreement with experimentally obtained mean arterial and venous pressure responses to acceleration, the procedure now was to adjust the bias on the PLL indicator comparator to obtain agreement with this new experimental data at one point of the tolerance curve.

Having made this adjustment, the parameters of the model were now defined. The test of the model was then to determine if it gave agreement with experimental data at other points of the tolerance curve with no further parameter adjustments. Figure 3 shows the closeness with which the CDRI model was able to match the experimental data. A special repetitive operation feature of the analog computer was used to good purpose in obtaining this data. This feature enabled the total time history of the system response to the haversine forcing function to be viewed immediately on an oscilloscope. By thus adjusting the peak G for each haversine period, the minimum value to produce PLL was quickly obtained.

The model not only provides the peak G at which the end-point occurs but also the time and duration of the end-point. In order to be consistent over the entire curve a 2 second PLL duration time was chosen. Most of the experimental data was of this order of magnitude. It was found necessary to add a time delay of 1 second to the results to bring about time agreement with the experimental data at the one point of the tolerance curve. This disagrees somewhat with the following statement: "Brain function and vision can be sustained at any G level for 3 seconds because the oxygen store within the brain tissue is sufficient to maintain adequate metabolism for this period of time even after the circulation has been cut off completely" (8). Having set this delay in the model, it was again checked for agreement with experimental data at other points of the tolerance curve.

In Figure 4 the percentage of time from the peak G to the midpoint of the PLL to the time from peak G to end of run (half period of haversine) was plotted against the half period of the haversine. Close agreement was again found between the experimental data and the CDRI model. The midpoint time of the PLL was chosen because some variation from the 2 seconds duration standard was found in the experimental data. The midpoint time was found to be invariant in the computer model for large variations in duration time. It is to be noted that, in the short period duration G profiles, the runs are over before the end-point occurs. Also, for the long period runs, the end-point occurs before the peak G is reached.

Having gained some confidence in the CDRI model after its agreement with experimental data for the haversine shaped G-profiles, the model was extended to study the effect of different shaped forcing functions. Figure 5 shows it being applied to a 4-second haversine G curve (2 seconds to peak) modified to hold at peak G for a prescribed length of time and then to return to base level in 2 seconds following the decline portion of the haversine curve. The figure shows a comparison between this shape of forcing function and the standard haversine forcing function. The results indicate that a tolerance curve based on the use of the total time from start of acceleration to the end-point for a measure of G duration regardless of the shape of the curve would be inconsistent.

A similar result was found when a ramp type forcing function was applied to the computer model. The results of this comparison study are shown in

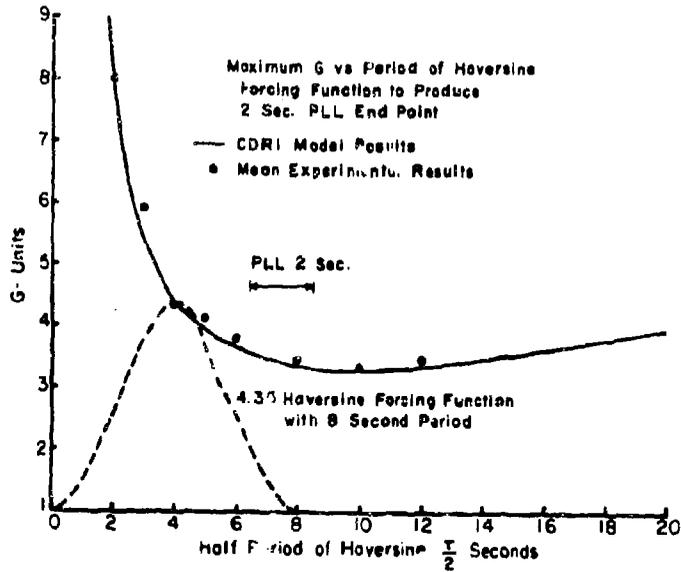


Figure 3. Maximum G vs. period of haversine forcing function to produce 2 sec PLL end point.

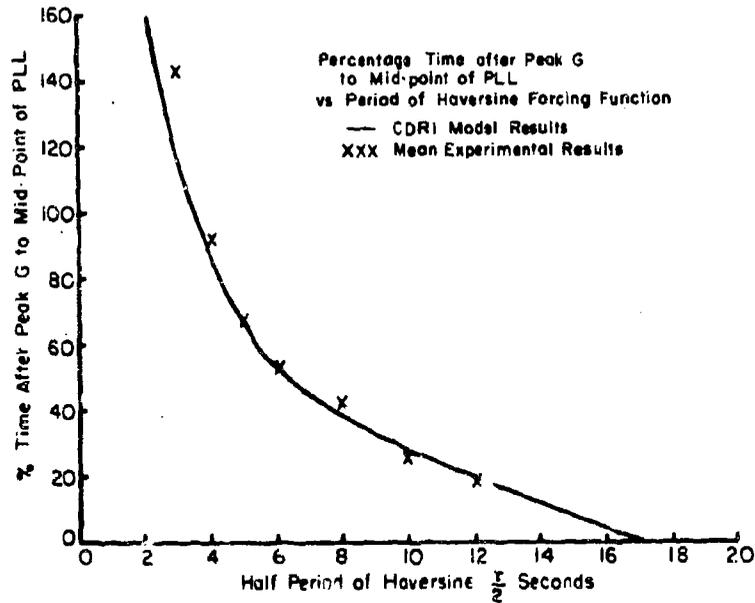


Figure 4. Percentage time after peak G to midpoint of PLL vs. half period of haversine forcing function.

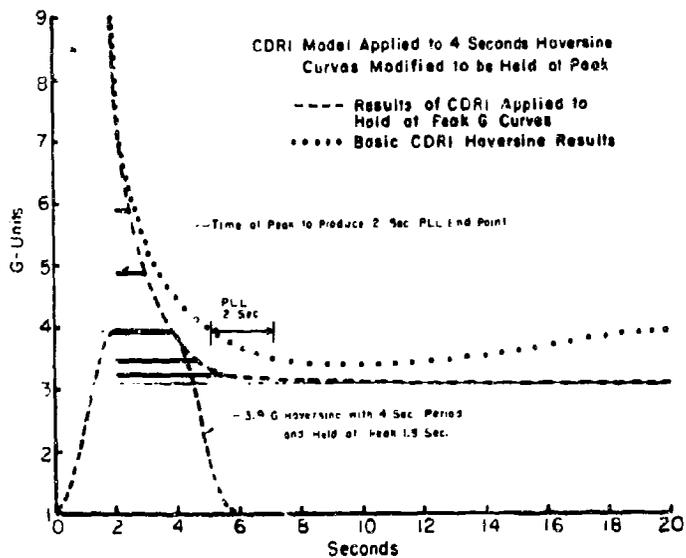


Figure 5. CDRI model applied to 4 second haversine curves modified to be held at peak.

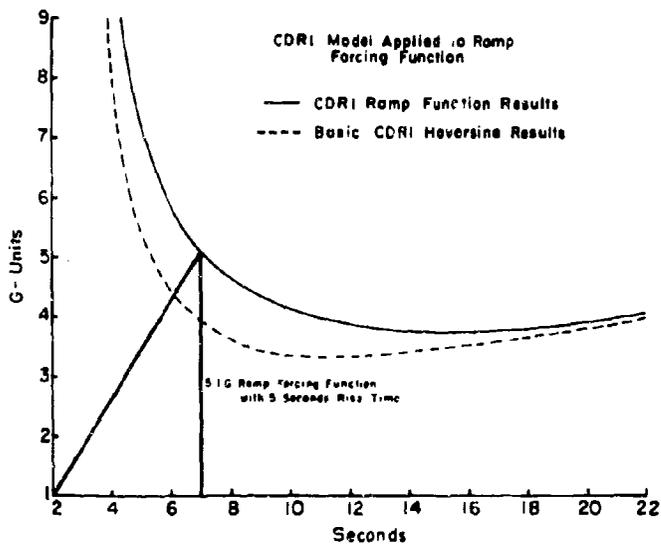


Figure 6. CDRI model applied to ramp forcing function.

Figure 6. A second significant finding of comparing a ramp forcing function with that of a haversine forcing function is that the decline portion of the G curve should not be ignored in assessing the total effect of a given G profile.

It has been found also, that close agreement is obtained between the CDRI model result and the G time-tolerance curve reported by Stoll (3) as shown in Figure 7 in the short period portion of the curve where the shape of the forcing function resembles that of a haversine. It is to be noted however, that in making this comparison a time shift had to be made to account for the fact that the time at which the end-point occurred from the start of the run was plotted and not the midpoint of the peak G occurrence as was done in the haversine curve results of Figure 3.

Although a 2 second peripheral light loss end-point was used in this study, the CDRI model is easily adaptable for different end-points such as CLL and unconsciousness by simply readjusting the bias on the indicator comparator. Also increased accuracy may be attained if the indicator is adjusted for each individual.

In addition to the application of the model to predicting human tolerance to complex forcing functions where it could be used on-line in computer simulation studies, it is an excellent tool for standardizing G time-tolerance studies and for assessing the importance of tolerance definition, G time duration, and the shape of the forcing function.

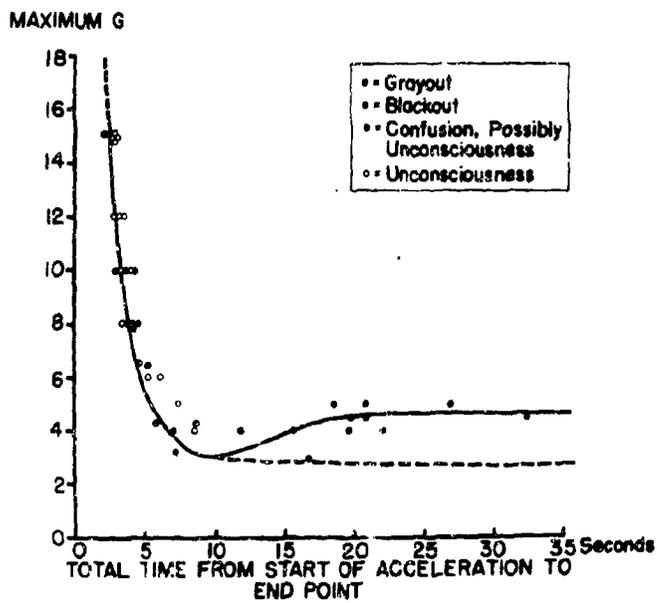


Figure 7. Human tolerance to positive G.  
 (From Stoll Report NADC-MA-5508)

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