DOES CARDIAC RHYTHM ALONE DETERMINE HUMAN BLOOD PRESSURE VARIATIONS?*

BY CARL J. WIGGERS, M.D.

(From the Physiological Laboratory of Cornell University Medical College,
New York.)

PLATES I TO 6.

INTRODUCTION.

The observation that blood pressure undergoes periodic variations with inspiration and expiration dates from the experiments of Stephen Hales (1) in 1733. Their nature and causes, though frequently reinvestigated, still remain subjects for physiological discussion. One phase of the question, the part played by variations in cardiac rate, is again considered in this investigation.

An extensive literature has grown about this question. Ludwig (2) observed these variations, placed the time of acceleration in the expiratory period, and disregarded its possible significance in the causation of pressure variations. It was held in similar disregard by Magendie (3), as well as by Donders (4). It remained for Ludwig's pupil Einbrodt (5) to show that in dogs the pressure rises in inspiration and falls in expiration. The increase in heart rate during inspiration, together with an increased blood flow through the thorax, was held to account for the inspiratory rise of pressure. Einbrodt, however, considered the first as of distinctly minor importance, for, after a rhythmic condition of the heart had been produced by vagus section, the blood pressure variations were frequently even increased.

Burden-Sanderson (6) confirmed the observation that the heart rate increased during inspiration. He believed that the enlargement of the thorax caused a belated expansion of the veins and the relaxing heart, which favored their filling. He reasoned that the more rapidly the cavities filled, the shorter the period of relaxation, the more vigorous its systole, and hence the higher the pressure.

Kowalewsky (7) and Zuntz (8) mention the variations of cardiac rate as contributing to the periodic blood pressure variations. François-Franck (9), Sommerbrodt (10), and Schweinburg (11) have made no reference to them in this connection.

Fredericq (12) demonstrated that probably these variations were dependent on a central influence and clearly analyzed the part they played in respiratory variations of blood pressure. He pointed out that variations of blood pressure occurred in the dog with respiratory phases, whether the heart was rhythmic or arhythmic. There was this difference: in the former case blood pressure fell

*Received for publication, August 26, 1913.
2 Does Cardiac Rhythm Determine Blood Pressure Variations?

during inspiration, in the latter it rose. He also pointed out that in animals where no normal variation in cardiac rate occurred (rabbit), the pressure always fell during inspiration. Fredericq, therefore, concluded that the mechanical influence of respiration tended to reduce arterial pressure during inspiration, but that in the dog these changes were overbalanced by an acceleration of the heart. Inasmuch as he observed a similar pulse variation in himself, he concluded that cardiac rhythm determined the direction of human blood pressure.

Various investigators, Riegel (13), Landois (14), Schreiber (15), Sommerbrodt (16), and others, using the sphygmograph as an indicator of blood pressure changes, concluded that, in man, a fall of pressure and not a rise occurred during inspiration. In 1886, however, Klemensiewicz (17) showed by simultaneous graphic records of respiration that the main change was a rise during inspiration which was preceded by a fall if cardiac acceleration was delayed in its onset. Werthheimer and Meyer (18) confirmed this and showed that atropin not only prevented the inspiratory cardiac acceleration but also the consequent rise in pressure. A glance at the published records of these investigators shows that only the lowest level of each pulse wave rises while the upper portion distinctly falls during inspiration. Such records tend to show that the cardiac rate determines the variation in diastolic pressure. Sphygmograph tracings taken from different individuals by other investigators, however, show both systolic and diastolic portions to vary as frequently in the same direction. While some of these variations may be attributed to individual variation, the point has been raised that the systolic and diastolic portions of sphygmograph records may not be regarded as a reliable index of the trend of pressure variations on account of the varying volume of the veins comites (Hill, Barnard, and Sequeira (18), and Hirschman (19)).

More recently Lewis (20) attempted to obviate these objections against the use of the instrument as a pressure indicator by suspending it from the wrist. From seventeen experiments upon this point, he concluded that the most frequent type of pressure variation during normal breathing is due to heart rate variation, systolic and diastolic pressure changing in the opposite directions as the heart slows and accelerates. During deep thoracic or abdominal breathing, however, another form of variation is added which is due to the mechanical influence of respiration.

Last year Erlanger and Festerling (21) showed that "the size of the sphygmomanometer oscillations" (i.e., diastolic pressure) "was not materially influenced by such pulse pressure changes as probably result from the changing systolic output," and further, that when breathing rate was voluntarily altered they followed the variations of respiration and not heart rate. A similar conclusion was arrived at by the mathematical analysis of Frank (22) who concluded that "moderate changes in the normal cardiac frequency can cause no change in blood pressure, since it already lies near the maximum." The writer (23) tested this question in the pulmonary circuit with the result that, within the range of cardiac cycle variation most commonly found in man (0.60 to 0.90), the length of the cardiac cycle was practically without influence on systolic and diastolic pressures as measured by an improved pulse pressure instrument.

This review establishes the idea that great variation in cardiac rate may determine entirely the trend of blood pressure changes.
It is generally admitted, however, that, in addition, there exists a mechanical influence due to respiratory movements which tends to exert a contrary influence on blood pressure and predominates when heart rate changes are not marked. It is not entirely agreed, however, whether the cardiac variations in man are great enough to exert any influence counteracting the effect of respiration itself, or whether there are individual variations.

Opposed to the current view as to the part played by respiration is that given in a recent communication by Henderson and Barringer (24). These investigators hold that it is impossible for the mechanical influence of respiration to modify arterial pressure except as it operates through a change in heart rate. Briefly stated their position is as follows: venous pressure in man and animals is always above a certain critical value, and therefore all beats of the mammalian heart are superimposable. This condition, however, is difficult to maintain in experimental animals and most experiments are performed with the venous pressure below the critical level. In such cases the most that respiration can do is to modify ventricular filling by periodically raising the venous pressure to a critical level, and arterial pressure may be modified independently of the rate. By special precautions (induction of hypercapnia and saline infusion), however, it is possible to preserve a critical pressure and reduplicate normal conditions. In such cases the systolic output and arterial pressure are determined solely by the length of the previous diastole. Henderson would harmonize the discordant observations as to whether the human pressure rises or falls in inspiration by saying that the change in cardiac rhythm bears no constant relation to these respiratory phases.

As this view rests upon experimental facts supporting the hypothesis that in normal animals it is physiologically impossible for mechanical influences of respiration to modify the blood pressure apart from changes in the heart rate, it becomes desirable to reinvestigate the question of how closely systolic and diastolic pressures in man vary with the duration of the previous heart cycles.

THE ESTIMATION OF HUMAN PRESSURE VARIATIONS BY THE SPHYGMOSCOPE OSCILLATIONS.

ANALYSIS OF PREVIOUS WORK.

The methods for detecting variation of human blood pressures have not been entirely satisfactory. They have been recently reviewed by Erlanger and Festerling (21) who, among other procedures, suggested a convenient method which may be briefly described as follows: The cuff of an Erlanger blood pressure apparatus was applied to an arm and the systolic pressure estimated. The pressure was then reduced five or ten millimeters, at which level a continuous record of pulsations, with the tambour attached to Erlanger's instrument, was recorded.
The method rests upon the principle that "if a pressure lying anywhere between systolic and diastolic be applied to an artery through a recording sphygmomanometer adapted to employ the principle of Marey, an oscillation is recorded whose amplitude is larger than that obtained at systolic pressure and smaller than that at diastolic pressure. If, while this pressure on the artery is maintained, . . . the intra-arterial minimum pressure should approach the extra-arterial pressure, the amplitude of the recorded waves should, as a result, increase; and vice versa, . . ."

It was, of course, evident to these investigators that the principle of Marey could be theoretically applied in this fashion to pressure measurements only provided that the pulse pressure were constant during consecutive beats of the heart, for upon the amplitude in pulse pressure the oscillations primarily depend. They, therefore, carried out animal experiments to demonstrate not only the validity of the theory that the amplitude of oscillations depended on the relation of extra-arterial to intra-arterial minimal pressure, but sought also to determine what modifying effect variations of pulse pressure exerted. Their conclusions on this point, here consecutively stated, were: (a) "Ordinarily, however, as experiments on animals demonstrate, pulse pressure changes do not mask blood pressure changes"; (b) "Nevertheless, one should keep in mind the danger of drawing conclusions from continuous blood pressure records without, at the same time, taking into consideration all of the factors at work in producing the changes"; and (c) in man, "the height of the oscillations is not materially influenced by such pulse pressure changes as probably result from the changing systolic output. . . ."

The experimental data, however, do not seem to establish satisfactorily the fact that these inferences may also be applied in cases where variation in the length of cardiac cycle is responsible for pulse pressure changes.

In the first place the records submitted show no satisfactory evidence that variations in diastolic pressure due to cardiac rhythm cause corresponding variations in the sphygmomanometer oscillations which may not as well be explained by pulse pressure variations or by the fact that the extra-arterial pressure was obliterating the vessel within the arteriograph. A case is pointed out by one of the authors (25) as bearing upon this point. For example, the systolic pressure

1 Erlanger, J., and Festerling, E. G., loc. cit., p. 381.
Carl J. Wiggers.

of the last vagus pulse of the second vagus stimulation in figure 3 in the article of Erlanger and Festerling rises almost to the same systolic level as the pulse following. The diastolic pressure of the former is far below that of the latter, yet despite the great difference in pulse pressure in favor of the vagus beat, the sphygmomanometer oscillations are distinctly smaller. To judge from the impact waves of the sphygmomanometer, however, the artery was entirely collapsed within the arteriograph during the vagus beat and not during the beat following, in which case no correspondence could be expected. Unquestionably, the lever throw during the vagus beat was greater than in the other beats recorded by the Hührlke manometer, so that the systolic pressure was actually less than that recorded in the vagus beats. This failure to control the fling of the manometer lever renders these records unsatisfactory evidence.

In the second place satisfactory evidence is not at hand to show that variations in pulse pressure due to heart rate changes do not mask blood pressure changes.

The fact that the lower diastolic pressure and increased pulse pressure accompanying vagus stimulation shown in figure 3 is attended by smaller sphygmomanometer oscillations is seemingly conclusive that the change in diastolic pressure chiefly determines the amplitude in oscillation and that pulse pressure changes play an insignificant part. Another explanation is more plausible, however. With the fall of diastolic pressure the systolic pressure also falls, and to judge from the typical impact waves of the sphygmomanometer record, it falls so low that the extra-arterial pressure is always obliterating the artery and, in consequence, this amplitude is necessarily smaller. During the first vagus stimulation when the diastolic pressure is practically the same, only the first three waves, in which the systolic pressure is somewhat higher, gave anything that might be called a sphygmomanometer record. As soon as extra-arterial pressure is no longer above intra-arterial, as shown in the third vagus stimulation, we get, allowing for friction irregularities, a correspondence between oscillations and pulse pressure changes.

Inasmuch as a clear decision in the matter is imperative to determine the influence of cardiac rhythm on blood pressure changes, it was deemed desirable to reinvestigate these questions.

EXPERIMENTS.

The sphygmoscope attachment of Erlanger's blood pressure apparatus was changed to the extent that a Frank's segment capsule, recording by a reflected band of light on a moving bromide film, was substituted for the tambour. By this change the quality of the apparatus was improved to such an extent that now, at least, the variations of pressure transmitted by the elastic ball of the sphyg-

moscope system were accurately picked up by the segment capsule and registered without friction on the writing surface. The sensitiveness was at the same time increased to such an extent that the pressure variations from the dog's femoral could be directly recorded. This was considered a distinct advantage, inasmuch as it is necessary in interpreting pressure measurements in man to deal with the elasticity coefficients of the overlying tissues and of the sphygmoscope system under different tensions and variable air contents. To this end, a conical cuff, containing a trapezoidal bag having a width of seven centimeters, was strapped to the thigh, and by special clamps so fastened to the tightly drawn skin that slipping was not possible. Preliminary tests showed that the pulsations in the artery peripheral to the bag, recorded by an exceedingly sensitive optical arrangement, were entirely prevented when the extra-arterial pressure was five to ten millimeters above the maximal pressure recorded from the other femoral by a maximum mercury manometer. In order to obviate the criticism, which according to the writer's opinion is unjust, that a considerably larger component of the pressure is lost in applying pressure to a flat and conical leg of a dog than by a cuff to the cylindrical arm of man, an arteriograph was applied to the carotid artery in three experiments. The variations in carotid pressure were recorded by Frank's optical manometer, while the maximum and minimum pressure was read as from the other femoral artery. The normal variations in heart rate, the effects of natural breathing, of cutting vagi and stimulating either end, of compressing the trachea, and of atropin and adrenalin as these bore upon the relation between the two curves, were all investigated.

The results of eight such experiments were conclusive. They fail to show that where a method is employed similar to that used in man, variations of diastolic pressure due to changes in heart rate determine variations in the amplitude of oscillations of the sphygmoscope. Specific instances are shown where an extra-arterial pressure not more than ten millimeters below maximal in the other femoral was applied by the bag to the artery. In figure 1 the size of the

8 In the later experiments the manometer was calibrated.
sphygmoscope oscillations 1 and 2 decreases when systolic pressure of the corresponding beat falls and the diastolic pressure remains unaltered (decreased pulse pressure). In figure 2 a progressive rise of diastolic pressure, due to an accelerated heart, causes not a larger but a smaller oscillation. In this case the highest maximal intra-arterial pressure reached was 167, the minimal was 75, and the extra-arterial was 150.

On the other hand, these records show that when variations in cardiac rhythm occur, an exact correspondence obtains between amplitude of oscillation and pulse pressure. Thus, in figure 1, when, during inspiration, the pulse pressure decreases, diastolic pressure remaining practically unchanged (waves 1 a, 1, and 2), the size of oscillations diminishes and what is of fundamental importance as showing the minimal determining influence of diastolic pressure, this relation held true for the entire range of extra-arterial pressures from above systolic to below diastolic. The three arteriograph experiments were particularly convincing upon this point. Records of experiments of which a few segments are shown in figure 3 illustrate this so clearly as to render detailed discussion superfluous. Experiments taken from the animal's leg with a cuff showed the same relations when the animal was in apnea, but, as the results of table I indicate, the movements incident to respiration in the dog occasionally impair an exact correspondence. The results are appended to show that even when extraneous influence sometimes impairs the results, the relation of the external to the diastolic pressure is always without effect in altering the relation between pulse pressure and sphygmomanometer oscillations. Inasmuch as a decrease in pulse pressure associated with a shorter cycle means a higher diastolic pressure, it follows that, contrary to the interpretation of Erlanger and Festerling, an increase in diastolic pressure in such cases is indicated by the smaller pulse pressure waves. It is necessary to lay stress upon this because the diastolic pressure changes will be misinterpreted when cardiac rhythm is not regular, if the size of the oscillations is taken as the criterion of diastolic pressure. This, of course, does not necessarily imply that larger oscillations may not accompany a rise of diastolic pressure. Figure 1, waves 3 and 4, show that, during natural breathing when
Does Cardiac Rhythm Determine Blood Pressure Variations?

<table>
<thead>
<tr>
<th>Observation</th>
<th>Maximal intra-arterial pressure</th>
<th>Minimal intra-arterial pressure</th>
<th>A. Variation in diastolic pressure (Frank's manometer)</th>
<th>B. Variation in pulse pressure (Frank's manometer)</th>
<th>C. Variation in size of oscillations (sphygmomanometer)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>126</td>
<td>130</td>
<td>+       +       +       +       +</td>
<td>+       +       +       +       +</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>96</td>
<td>-       -       +       -       +</td>
<td>-       -       +       -       +</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+       +       +       +       +</td>
<td>+       -       +       -       +</td>
<td>C</td>
</tr>
<tr>
<td>3</td>
<td>128</td>
<td>152</td>
<td>+       +       +       +       +</td>
<td>-       -       +       +       +</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>98</td>
<td>-       -       +       +       +</td>
<td>-       -       +       +       +</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+       +       +       +       +</td>
<td>+       -       +       -       +</td>
<td>C</td>
</tr>
<tr>
<td>4</td>
<td>118</td>
<td>118</td>
<td>+       +       +       +       +</td>
<td>+       +       +       +       +</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>92</td>
<td>-       -       +       +       +</td>
<td>-       -       +       +       +</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-       +       +       +       +</td>
<td>+       -       +       -       +</td>
<td>C</td>
</tr>
<tr>
<td>5</td>
<td>118</td>
<td>100</td>
<td>+       +       +       +       +</td>
<td>+       +       +       +       +</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>90</td>
<td>-       -       +       +       +</td>
<td>+       +       +       +       +</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-       +       +       +       +</td>
<td>-       -       +       +       +</td>
<td>C</td>
</tr>
<tr>
<td>6</td>
<td>118</td>
<td>90</td>
<td>+       +       +       +       +</td>
<td>-       +       +       +       +</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>88</td>
<td>-       -       +       +       +</td>
<td>+       +       +       +       +</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>-       +       +       +       +</td>
<td>-       -       +       +       +</td>
<td>C</td>
</tr>
<tr>
<td>7</td>
<td>80</td>
<td>88</td>
<td>0       +       -       -       +</td>
<td>0       +       -       -       +</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0       +       -       -       +</td>
<td>0       +       -       -       +</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0       +       -       -       +</td>
<td>0       +       -       -       +</td>
<td>C</td>
</tr>
<tr>
<td>8</td>
<td>138</td>
<td>70</td>
<td>+       +       +       +       +</td>
<td>+       +       +       +       +</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>90</td>
<td>+       +       +       +       +</td>
<td>+       +       +       +       +</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+       +       +       +       +</td>
<td>+       +       +       +       +</td>
<td>C</td>
</tr>
<tr>
<td>9</td>
<td>160</td>
<td>85</td>
<td>0       +       +       +       +</td>
<td>0       +       +       +       +</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>88</td>
<td>0       +       +       +       +</td>
<td>0       +       +       +       +</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0       +       +       +       +</td>
<td>0       +       +       +       +</td>
<td>C</td>
</tr>
<tr>
<td>10</td>
<td>160</td>
<td>160</td>
<td>0       +       +       +       +</td>
<td>0       +       +       +       +</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>88</td>
<td>0       +       +       +       +</td>
<td>0       +       +       +       +</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0       +       +       +       +</td>
<td>0       +       +       +       +</td>
<td>C</td>
</tr>
</tbody>
</table>

the heart is regular, large oscillations often accompany an increase in diastolic pressure, but the greater coincident pulse pressures may account for the changes. Nor do these experiments necessarily disprove the possibility that the amplitude of oscillation may be determined by the relation of intra-arterial diastolic pressure to extra-arterial pressure when heart rate and pulse pressure remain unaltered. Inasmuch as such conditions are rarely approximated in man, however, they scarcely permit the application of the criterion to establish human pressure variations.

* + = an increase; — = a decrease over the preceding wave; 0 = no change.
Since variations in amplitude of oscillations parallel changes in the pulse pressure, it became desirable to investigate whether the troughs and crests of the sphygmoscope oscillations registered by photographic means follow variations in systolic and diastolic pressure of Frank's manometer. If the volume changes of an artery induced by a pressure variation within the vessel could be transmitted to an ideal manometer system externally applied and sustaining a pressure less than systolic, they would induce similar but much smaller changes in this manometer. If these could be recorded without error, they would be proportionate to the variations of intra-arterial pressure. Hürthle (26) attempted to apply this principle in exact estimation of human pressures. Although Frank (27) has pointed out that this can not be realized with such a method, it may still be conceived that an instrument of much lower quality may show a directional but not a quantitative change in pressure.

A comparative study of animal experiments shows that, during apnea, e. g., after curare, during central vagus stimulation, and after adrenalin, an exact qualitative but by no means a quantitative correspondence exists. The troughs and crests, beat by beat, change in direction with the diastolic and systolic pressures of Frank's manometer (figure 2). This correspondence holds not only when the extra-arterial pressure is equal to the diastolic within the artery but is equally faithful up to the systolic level.

A study of the arteriograph records, during which animals were breathing, showed also a general correspondence in the variations of the sphygmoscope record and Frank's manometer (figure 3). Many isolated exceptions were present, however, in the records taken from the leg which it is necessary to analyze in order to recognize the limitations of the method in man. Thus in figure 1, to judge from waves 1 and 2 of the sphygmomanometer record, both systolic and diastolic pressures are falling. A glance at the corresponding pressure waves shows, however, that systolic pressure alone fell in wave 1 and rose again in wave 2. Again, wave 4 gives the impression that an increase in both systolic and diastolic pressure over the preceding beat occurred, whereas the direct pressure record shows that systolic pressure decreased and diastolic pressure remained unchanged.
An analysis of the cases where discrepancies occurred showed that they could be referred to extraneous movements imparted by respiratory or voluntary muscular contractions of the limb to the bag. The latter are easily recognizable on the curves from animals and man (figure 4), and when present the records may be discarded. The respiratory variations are not always so clearly shown (figure 1), and in the dog they are exceedingly difficult to obviate since every respiration exerts a tug upon the skin of the thigh throughout the inguinal fold of skin connecting the abdomen with the thigh. It follows that the troughs and crests of individual sphygmomanometer variations follow the direction of systolic and diastolic pressures within the artery accurately only when extraneous influence can be guarded against. The experimental plan of the method, therefore, shifts to man.

Fortunately, on account of anatomical differences, these movements can probably be controlled with attention to a proper placement of the arm. If an arm bag is applied to the arm hanging to the side, one may obtain marked variations of the whole curve with respiratory movements which disappear entirely or become altered in direction when the arm is allowed to rest comfortably in a horizontal position away from the chest. In control experiments no variations that could be attributed to such an influence were discernible when a second narrow cuff with a pulse-obliterating pressure was placed above the recording cuff.

It may be concluded then, that, during natural breathing, when precautions are taken that no extraneous movement is transmitted to the cuff, the crests and troughs recorded by an air-tight sphygmoscope system give respectively a directional indication of systolic and diastolic pressures occurring in man.

THE RELATION BETWEEN SYSTOLIC AND DIASTOLIC PRESSURES AND THE LENGTHS OF THE CARDIAC CYCLES IN MAN.

Method of Experimentation.—The subjects reclined upon a bed, their left arms, strapped with a blood pressure cuff, resting away from the thorax. Each subject unacquainted with the objects of the experiment was allowed to rest quietly for several minutes. The systolic pressure was then roughly determined by palpating for
the return of the radial pulsation and the instrument set so that the pressure was 10 to 15 millimeters below this level. The oscillations of the sphygmoscope transmitted by an air-tight system to a Frank's segment capsule, together with the movements of a respiratory tambour communicating with a pneumograph and a tuning fork with a vibrating period of 0.02 of a second, were then projected upon a moving bromide film.

As a rule, the breathing of these quietly resting subjects was entirely involuntary and shallow. When a record had been obtained under these conditions the subject was told to breathe perfectly naturally. The psychic element thus introduced resulted, without fail, in deepening the breathing. This respiration, however, did not exceed in depth that of the normal individual. It is designated as voluntary respiration to distinguish it from the involuntary type naturally assumed. In a number of cases the effects of deep breathing and apnea were also recorded.

Method of Analyzing the Results.—The developed records obtained from thirty-five different subjects were analyzed as follows: The cardiac waves were consecutively numbered and their relation to inspiration and expiration was determined. The duration of each cardiac cycle was next expressed in hundredths of a second. By the aid of the millimeter scale photographed on the film, the relative relations of the troughs and crests of the waves were directly determined and expressed in terms of millimeters (figure 5).

These figures, which, according to previous discussion, could give only a criterion of qualitative changes in systolic and diastolic pressures occurring during consecutive beats, were plotted on the ordinates of cross-section paper. To facilitate plotting, the beats were laid off as equal lengths on the abscissae, the actual duration of the cardiac cycle being numerically indicated for each wave. In this way it was possible to study whether the variations in diastolic and systolic pressures of consecutive waves accorded with those expected.

As the relative changes in systolic and diastolic pressures were alone of importance the actual figures have been omitted from the plot.

The diastolic pressure for any wave (e.g., wave 1, figure 1) is considered throughout the paper as the lowest pressure reached previous to the systole of that beat (point a), and the term systolic pressure is applied to the highest pressure reached during the systole of that beat (point b).
Does Cardiac Rhythm Determine Blood Pressure Variations?

pected, provided the length of the preceding cardiac cycles solely determined these pressures. In order to do this it is essential to bear constantly in mind the anticipated effects of any change in heart cycle.

It is generally recognized that a lengthening of the cardiac cycle increases, and a shortening decreases the mean pressure of the succeeding beat. This, however, only imperfectly relates the pressure effects, since the inference might be drawn that both systolic and diastolic pressures necessarily follow the directional change of the mean pressure, which is not always the case in animals. When, for example, variations in cardiac rate solely determine the blood pressure changes in anesthetized animals in apnea, as shown by Frank’s mirror manometer (N = 170), it is the rule that shortening of a cardiac cycle increases the diastolic and decreases the systolic pressure of the beat following (figure 2, a and b). The same changes occur in naturally breathing animals when cardiac rhythm controls the pressure (figure 7). The systolic pressure deviates from this rule, however, (a) when peripheral constriction is great (after adrenalin or asphyxia), (b) when the shortening of the cycle is not sufficient to alter the degree of filling (in very slow heart beats), and (c) when a progressive acceleration lasts for a considerable period so that the systolic pressure is supported by the diastolic (figure 3, c, d, e). Conversely, a lengthening of the cardiac cycle causes an elevation of the systolic and a fall of the diastolic pressure of the following beat. Here also the systolic pressure may fall under conditions opposite to that outlined above. In all cases, however, the pulse pressure decreases when the heart accelerates, and increases when it slows.

In dogs with rhythmic hearts, or where respiration controls the pressure variations, inspiration causes a fall of both systolic and diastolic pressures, and expiration a rise (figure 1). The pulse pressure increases during expiration and decreases during inspiration. Systolic and diastolic pressures change in the same direction.

Results.—To facilitate an analysis the experiments were grouped in accordance with the points they illustrated, and from these groups a number of representative plots are briefly discussed (figure 8).
Influence of Heart Cycles During Apnea.

Experiment 32.—Breath held in expiration. Very slight variations (0.01 of a second) in rhythm occur and the systolic and diastolic pressure of consecutive beats do not vary.

Experiment 35.—Voluntary apnea. Heart cycles increase in length slightly (0.02 of a second). This is without influence on systolic pressure, but a slight decrease in diastolic pressure is evident. At the fifth beat, i.e., after a series of progressively lengthening beats, the systolic pressure falls, due to lack of diastolic support.

Experiment 33.—Voluntary apnea with very slow heart rate. A lengthening of the third cycle plotted causes a fall of diastolic pressure and a decrease in the systolic pressure of the fourth wave. A shortening of the fourth cycle in the fifth wave increases both diastolic and systolic pressures.

Experiment 36.—Voluntary apnea. Average cardiac cycles. A progressive decrease of the cardiac cycles during the first five waves results in a progressive rise of diastolic and a fall of systolic pressures. At the sixth and seventh waves, the systolic pressure rises, due to increased diastolic support resulting from a continued decrease in length of heart cycles. As the cycle increases again in the seventh wave, the diastolic pressure decreases, but systolic does not rise for a beat, probably because the systolic pressure was already high due to diastolic support.

Experiment 37.—Voluntary apnea. A progressive and pronounced lengthening of the heart cycle takes place. The progressive decrease of diastolic pressure is accompanied by a systolic rise in the first three waves. The systolic pressure does not continue to rise on account of the greater diastolic drop and, for the same reason, it falls in the sixth and seventh waves.

These experiments, which were the only ones in a series of twenty apnea experiments in which marked cardiac variation occurred during apnea, show that when respiration is in abeyance, variations of cardiac rhythm, except when very small, modify the pressures of man in precisely the same manner as was above stated to be the case in animals.

From this the rule may be formulated that the duration of the preceding cycle probably cannot be considered to govern the pressures unless it can be shown that:

1) a decrease in systolic pressure is (a) preceded by a cycle shorter than that of the wave before (e.g., waves 4 and 5, experiment 36), and accompanied by an increase of diastolic pressure, or (b) preceded by a cycle of the same or a longer length than that of the wave before, and by a decrease of diastolic pressure for several previous beats (e.g., waves 5, 6, and 7, experiment 37); and,

2) an increase in systolic pressure is (a) preceded by a cycle
Does Cardiac Rhythm Determine Blood Pressure Variations?

longer than that of the wave before and accompanied by a decreased diastolic pressure (e.g., waves 2 and 3, experiment 37), (b) preceded by a cycle of the same or a shorter length than that of the wave before, and by an increase of diastolic pressure for several previous beats (e.g., waves 6 and 7, experiment 36).

INFLUENCE OF RESPIRATION WITHOUT CHANGES IN CARDIAC RHYTHM.

Experiment 21.—Involuntary breathing, moderate depth. After the first wave plotted the cardiac cycles are equal. In spite of this fact systolic pressure falls distinctly during inspiration.

Experiment 17.—Involuntary breathing, moderate depth. The duration of the cardiac cycles determining the first five beats is practically uniform. In spite of this the systolic pressure undergoes a fall during inspiration and a rise during expiration which can only be accounted for as an influence of respiratory movement on blood pressure.

Experiment 24. Curve A.—Involuntary breathing, moderate depth. Although the heart cycles are equal, systolic pressure is somewhat lower during inspiration and higher during expiration. Curve B.—Voluntary, deeper breathing. The inspiratory phase is prolonged and the fall of both systolic and diastolic pressures during this phase is more prominent. Since the cardiac cycles determining waves 2 and 3 and also 4 and 5 are of the same length, the pressure change may be attributed to the effect of inspiration. The pressure changes of wave 6, on the other hand, might be attributed to a cardiac influence.

The experiments, of which these are illustrations, show that, in cases where cardiac variations are negligible or absent, mechanical respiratory influences lower the systolic pressure when breathing is shallow, and the diastolic pressure also when breathing becomes somewhat deeper. As in animals, systolic and diastolic pressures vary in the same direction.

INFLUENCE OF SLIGHT VARIATIONS IN CARDIAC RHYTHM DURING NATURAL RESPIRATION.

Experiment 35. Curve A.—Shallow, involuntary breathing. A fall of systolic pressure during inspiration occurs. Cardiac rhythm is not responsible for the change because the fall of systolic, with a slight tendency to a rise of diastolic pressure, follows a consecutive lengthening of the cardiac cycles; and although a variation in the duration of the cardiac cycle occurs during the two beats of inspiration, the pressure remained unaltered for these beats. Curve B.—Deeper voluntary breathing. Waves 2, 3, 4, and 5 might be accounted for by cardiac rhythm, but the systolic decrease of the sixth wave could scarcely be attributed to the lengthened cycle preceding it, nor could the fall of diastolic pressure for the seventh wave be accounted for by the shorter cycle of wave 6.

Experiment 22. Curve A.—Shallow, quiet breathing. A very slight reduction of systolic pressure coincident with inspiration occurs. The slight variations
of waves 1, 2, 3, and 4 during expiration are easily explained by heart rate variations. The fall of systolic pressure of wave 5, though slight, cannot have been due to such variation. Curve B.—Voluntary breathing. The sudden increase in systolic pressure of waves 3 and 4 could not possibly be attributed to heart rate variations. Nor could the fall of systolic and diastolic pressures during waves 7 and 8 be referred to the shortened cycles preceding them.

Experiment 19. Curve A.—Shallow, involuntary breathing. The shortest cardiac cycles do not appear during inspiration and the cardiac cycles determining the first to the fourth waves are practically of the same duration. Still the systolic pressure falls during inspiration. The shortest cycles occur in expiration where wave 5 is followed by an unexpectedly high systolic pressure with no corresponding increase in diastolic pressure. Upon increasing the depth of respiration (curve B), the systolic and diastolic pressures follow the respiratory phases exactly. The determining cycles for waves 2 and 3 do not vary greatly, yet systolic and diastolic pressures both fall. Waves 4 and 5, determined by the same cycles, show a pronounced difference in pressure not to be accounted for by rate variation.

Experiment 30. Curve A.—Quiet, involuntary breathing. The systolic pressures of waves 2 and 3 during inspiration are equal yet determined by different period cycles. The cycles governing waves 4 and 5 in expiration are equal, but both systolic and diastolic pressures increase in the latter beat.

Experiment 30. Curve A.—Quiet, involuntary breathing. Every pressure
change can be explained by a variation of cardiac rhythm. That respiration has a modifying influence, however, is suggested by the fact that, although the systolic and diastolic pressures of waves 5 and 6 both rise, the pulse pressure is greater. *Curve B.*—When breathing becomes deeper, respiration alters the direction of the pressures, as determined by heart rate variation. The lower systolic pressure of waves 4 and 5 and the higher systolic pressure of wave 6 are directly opposite to those expected if determined by previous heart cycles. The diastolic pressure also fails to agree with heart rate variation.

These cases show that when a considerable variation in cardiac rhythm occurs, especially when cardiac acceleration is limited to inspiration, a casual glance leaves the impression that systolic and diastolic pressures are entirely governed by the previous cardiac cycle. A careful perusal, however, shows that in each case one or more beats occur during every shallow respiration that cannot be accounted for upon this basis, and, in many cases, when breathing becomes deeper the effect of respiration becomes dominant.

**MARKED RESPIRATORY ARHYTHMIA.**

*Experiment 29 A.*—Moderately deep, involuntary respiration. Variations in cardiac cycle (0.23 of a second) entirely accounted for many waves not plotted. Wave 2, during inspiration, is governed by the same cycle as wave 1 in expiration, but the latter has a much reduced systolic pressure. The reduced systolic and increased diastolic pressure of the other waves in inspiration may, however, be accounted for by cardiac variations. Waves 5, 6, and 7, having practically cycles of the same length, show an increase of both systolic and diastolic pressure during expiration. It is interesting to note that wave 2, governed by a heart cycle of 0.83 in inspiration, is no larger than wave 7 governed by a cycle of 0.61 in subsequent expiration.

*Experiment 16.*—Moderate deep, voluntary breathing, cardiac cycle variation 0.23 of a second. With a progressive decrease of the cardiac cycle we find a decrease in systolic and an increase in diastolic pressure. The low diastolic pressure of wave 6 and the higher systolic pressure of wave 7 are difficult to accredit to the shorter cycles preceding.

*Experiment 13.*—Involuntary, moderate breathing, cardiac cycle variation 0.30 of a second. The variations of both systolic and diastolic pressures correspond to cardiac variations entirely. Wave 3, following a longer cycle, shows the characteristic lower systolic pressure which is the rule in slow hearts. A respiratory influence may exist but its invocation to explain the changes is not necessary.

*Experiment 7.*—Moderate deep respiration, cardiac variation 0.29 of a second. Systolic and diastolic pressure can be accounted for by heart rate variation. The rise of diastolic and fall of systolic with consecutive shortening until after the fifth wave leads to an increase of systolic pressure due to summation, is typical of cardiac rate changes. No necessity exists for the assumption of intervention by respiration.

*Experiment 18.*—Dog trained for calorimeter work. Figure 7 shows the
characteristic pressure variations of the normal, unanesthetized dog. Such pronounced variations in rhythm are never encountered in man. With inspiratory acceleration the diastolic pressure rises and systolic pressure falls until after several beats the summated effect causes the systolic pressure also to rise slightly. No evidence is found that mechanical movements of respiration play a part.

It may be concluded that in cases where extreme variations in cardiac rhythm occur these variations often obscure entirely any effect that movements of respiration may have on the systolic and diastolic pressures.

CONCLUSIONS.

Changes in cardiac rhythm are not the only determinants of blood pressure variations in man. They play a part in the variations of systolic and diastolic pressures, the relative importance of which depends on the degree of arhythmia present and on the depth of respiration which, in itself, causes the systolic and diastolic pressures to decrease during inspiration and increase during expiration. No degree of rate variation can be regarded as a type. The cases range from those in which respiration governs the change of pressures entirely through those where more or less complicated mixtures of heart rate and respiratory influences intermingle to those in which extreme cardiac variations alone determine the pressure changes.

The emphatic insistence of Henderson and his collaborators that heart rate changes play a more important part than is commonly recognized in man is true in many cases. That, in certain cases, it is the only determining influence may also be admitted, but they are in the minority. The majority show the intervention of a respiratory influence which controls, at least, the variations of systolic pressure. In the light of these results, the doctrine that, in man, an effective venous pressure exists sufficient during all respiratory phases to insure superimposable beats, must be subjected to further reinvestigation. 7

BIBLIOGRAPHY.


Does Cardiac Rhythm Determine Blood Pressure Variations?

25. Erlanger, J., Personal communication.

EXPLANATION OF PLATES.

PLATE 1.

Fig. 1. Natural respiration. The amplitude of the sphygmoscope oscillations corresponds to pulse pressure changes and not to variations in diastolic pressure. Troughs and crests fail to follow intra-arterial systolic and diastolic pressures if breathing movements are communicated to limb. R = respiration, inspiration up-stroke; P = carotid pressure recorded by Frank's optical manometer; S = sphygmoscope oscillation. The numbers are referred to in the text. About three fourths actual size.

Fig. 2. Apnea. Close correspondence of troughs and crests of sphygmoscope record with systolic and diastolic changes recorded by Frank's manometer. The lettering is the same as in figure 1. About two thirds actual size.

PLATE 2.

Fig. 3. Five segments of records, showing that variations of pulse pressure occasioned by rhythmic cardiac changes determine the amplitude of the sphygmoscope oscillations obtained from an arteriograph. In the upper curve alone, where the intra-arterial systolic pressure fell below extra-arterial, and conse-
FIG. 1.

FIG. 2.

(Wiggers: Cardiac Rhythm.)
Fig. 4.

(Wiggers: Cardiac Rhythm.)
quently obliterated the vessel, does a fall of diastolic pressure together with an increase of pulse pressure result in smaller oscillations. The lettering is the same as above. B = the base line from the top of which calibration was made, hence the calibration scale on Frank's pressure record (P) applies to the top of the line. About two thirds actual size.

PLATE 3.

FIG. 4. Three segments of records showing at X the effect of extraneous muscle contractions, (A) in the dog, and (B and C) in man. Actual size.

PLATE 4.

FIG. 5. Human pressure variations, involuntary shallow breathing, slight heart rate changes. T = time in 0.02 of a second. R = respiration, inspiration upstroke. S = sphygmoscope oscillations. V. P. = jugular pulse, of no significance in present connection. About five sixths actual size.

PLATE 5.

FIG. 6. Human pressure variations, involving quiet breathing. Average rhythm variation. The lettering is the same as before. About five sixths actual size.

FIG. 7. Pressure variations of an unanesthetized dog resting and breathing quietly. Marked cardiac arrhythmia. About actual size.

PLATE 6.

FIG. 8. Plots from experiments showing the relation of systolic and diastolic pressures to heart cycles and respiration.