Some Characteristics of Certain Reflexes Which Modify the Circulation in Man

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Records are presented which have been obtained from man by direct intra-arterial catheterization and electrocardiography. These records have been selected (1) because they offer evidence for the validity of Starling's law in intact man and (2) because they demonstrate that when the heart is influenced by activity of the so-called "intrinsic" reflexes these manifestations of Starling's law are modified. It appears from these types of data that ventricular activity may be directly affected independently of influences upon the pacemakers of the heart.

INTRODUCTION

DURING THE past three to four years direct intra-arterial pressures have been obtained from almost 1000 persons. The method employed a tiny flexible tube inserted into an artery and then connected to a capacitance manometer and the pressure curves were recorded by means of an ink writer. This system permitted the observation of accurate records of the pulse contour over long periods of time without discomfort to the subject. Also, by observing the ink writer, changes in the circulation which follow stimuli could be at once identified. Such observations were carried on during a variety of conditions such as general or local anesthesia, surgery, many conditions of disease in its various stages and during certain physiologic and pharmacologic experiments.

While many of the periods of recording were not planned as such, in one way or another many of the conditions of certain classic physiologic experiments formerly performed on animals were hereby repeated on man. The results obtained on man, however, were by no means always concordant with the expectations from the classic animal experiments. This was especially true of the effects of carotid sinus stimulation upon the heart and circulation as well as other reflex effects arising from stimulation of the visceral mesentery. The evidence strongly suggests that such reflex pathways mediate activity which modifies the manifestation of Starling's law and which appear to affect the ventricle directly. These changes appear both with and without influence upon the pacemaker. Also, interesting observations have been made of the manner in which the pulse rate responds to circulatory alterations under certain conditions. It is the physiologic aspect of these observations which will be stressed in this presentation.

METHODS AND TYPE OF DATA

The method used for intra-arterial pressure measurements has been described elsewhere. The fidelity of the system is such that accurate and linear recordings can be obtained from intra-arterial pressure changes to give true pulse contours. This type of recording also eliminates the errors inherent in the Riva-Rocci method.

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* It is not the purpose of this paper to evoke a discussion of the validity of pulse pressures and contours as a representation of stroke volume. Suffice it to say that this author feels, as do others, that the available evidence is such that, if one considers the contour as well as the pressures present in the accurately recorded arterial pulse wave, one is justified in using the data presented in the manner set forth in this paper. The available evidence indicates that the changes in pulse contour during its transmission from aorta to brachial artery are such that the criteria used with the aortic pulse may be used also for the brachial pulse. In any event, the ballistocardiograph is the only other device or method allowing judgment of beat to beat changes in stroke volume. The type of data reported here could not have been obtained from direct Fick measurements.
Electrocardiograms have been obtained with a direct recording Sanborn Electrocardiograph.

DATA AND DISCUSSION

I. Manifestations of Starling's Law in Man.

Figure 1 demonstrates typical effects following extra systoles. It should be noted that following the extra systole there is a period of prolonged diastole. The next beat is more forceful as is evidenced by an augmented pulse pressure and a contour indicating a larger stroke volume. We are justified in thinking that increased cardiac distention from the prolonged filling time caused the increased response in accord with Starling's law.

Although the records shown were obtained from a hypertensive patient, they were selected because the same effect was demonstrated at all pressure levels and under differential spinal anesthesia. Similar records have been obtained from over 200 individuals with normal cardiovascular systems and under various anesthesias and in many stages of anesthesia. Premature contractions and dropped beats in otherwise normal rhythms are perhaps the simplest events producing prolonged diastole independ-

![Figure 1](https://example.com/figure1.png)

**Fig. 1.** Effects which follow extra systoles. These records were obtained from a 52 year old hypertensive patient. Upper left section obtained while patient was lying quietly on the tilting ballistocardiograph table. In this section 7 extra systoles which are followed by periods of prolonged diastole, then markedly stronger pulses, may be seen. These effects may also be seen in the upper right section which followed tilting to 70°, head up. The patient was then given a differential spinal anesthesia to a sensory level of D-4. Note that at all pressure levels a prolonged diastolic period is followed by a stronger contraction. It may also be noted that the pulse rate does not accelerate following the hypotension produced by differential anesthesia in this patient. In this case it may also be seen that there is not a marked alteration in the slopes of the pulse curves. All vertical lines represent 1 second except in the lower right section where the paper speed was 25 mm./second, i.e. each vertical line represents 0.20 second.

II. Reflex Effects Which Modify the Strength of Myocardial Contraction.

A. Carotid Sinus Reflexes. Figures 2 and 3 show the effects following prolonged diastole by carotid sinus stimulation. It is to be noted that the prolonged filling time is not followed by a more forceful contraction under these conditions. In all cases in man where we have been able to produce bradycardia by stimulat-

ing the carotid sinus, the period of prolonged diastole is followed by a less forceful contraction as evidenced by a smaller pulse pressure and altered contour. This effect is independent of the type of conduction; it occurs in complete heart block as well as in simple prolongation of the P-R interval.

It seems most likely that this unexpected response was due to a primary weakening of the ventricular myocardium so that it did not respond to an increased filling with an increased output. Other alternatives have been considered: (1) A stronger contraction might have taken place with its effect on the pres-
sure pulse masked by concurrent changes in arterial distensibility; experience with pulse wave velocity measurements\(^5\) and examination of the effect of a stronger contraction. (2) A simultaneous decrease in cardiac filling might have prevented a beat of increased strength.

Fig. 2. Effects following stimulation of the carotid sinus. Intra-arterial and electrocardiographic records were obtained during an operation designed to denervate the left carotid sinus in a patient with complete heart block who had suffered a number of Stokes-Adams attacks following pressure on the sinus area. At operation no tumor could be found in the area and microscopic examination of tissue showed no structural abnormality. Extensive examinations including ballistocardiograms failed to uncover any co-existing disease or abnormality of the myocardium.

Upper record demonstrates the prolonged periods of asystole which followed stimulation of the carotid sinus. All such periods in this patient followed an extra systole. The vertical lines represent 1 second. The next lower record is Lead III of the simultaneous electrocardiogram (heavy vertical lines represent 0.20 sec.). Note that during the asystole the P waves continue at their regular rate. The third and fourth sections (time marked as in strip 1) demonstrate that asystole follows stimulation within one to two seconds. The number 105 seen in the fourth record identifies a run of a form of ventricular tachycardia which is also seen in the lower electrocardiographic record. Note that during this period of tachycardia the mean blood pressure does not continue to fall; however a Riva-Rocci determination would not give a blood pressure since the pulses are too small to give an audible sound. Atropine (1.2 mg.) was given intravenously one minute before the lower record was obtained. While the effect of atropine is somewhat equivocal, it may be seen that the pulses following prolonged diastole are not as markedly weakened as are those in the records obtained previously.

Sections of the records indicates, however, that this is apparently not effective in that degree. Also the pulse contour and the pressures at the end of prolonged diastole indicate that marked peripheral vasodilatation did not mask following the prolonged diastole in many of these instances. But during carotid sinus stimulation the neck veins became evident as a result of distention; also, with periods of diastole lasting 15 to 18 seconds, cardiac fill-
ing would have to cease almost completely in order to prevent some increased cardiac number of beats. That the overdistention of the heart could cause the weakened response also seems unlikely. In the Valsalva experiment cardiac filling is almost certainly augmented, but an equivalent, prolonged di-

![Figure 3. Effects following stimulation of the carotid sinus. The upper record was obtained from a 37 year old man who had suffered no symptoms suggesting a hypersensitive carotid sinus; yet stimulation of the right sinus produced a period of prolonged diastole which was followed by a weakened contraction. Vertical lines represent 1 second except for the last three pulses during which time the lines are 0.20 second apart. Stimulation of the left sinus area was without effect.

The second, third and fourth sections were obtained during an operation designed to denervate the right carotid sinus in a 30 year old patient who had suffered syncopal attacks which would be reproduced by digital pressure over the area. The vertical lines in these records are 0.20 second apart.

The lower two records were obtained from a hypertensive patient who had not suffered syncopal attacks suggesting a hypersensitive carotid sinus. Note that the blood pressure and pulse pressure is depressed for a longer period than the pulse rate following stimulation. Note also that straining during the period of stimulation causes increases in the mean and pulse pressure. Subjects frequently respond to the rather uncomfortable digital pressure on their necks by straining. If Riva-Rocci determinations were made during these periods of strain the background hypotension would not be manifested. The vertical lines, again, are 1 second apart except for obvious periods when the paper was speeded to 5 times the original speed. Electrocardiograms were also obtained during these procedures; however they showed only a prolonged P-R and P-P interval.

distention. In addition, observations upon both man and animals have shown that the reduction in pulse and mean pressure which follows decreased cardiac filling, as by constriction of the vena cava, comes on gradually during a number of beats. (3)
astole is regularly accompanied by an increased pulse pressure. In addition the weak response occurs in some cases with relatively shorter periods of bradycardia following carotid sinus stimulation than is seen following extra systoles.

The want of a satisfactory alternative has led to the belief that carotid sinus stimulation causes not only an inhibition of the pacemaker but also a weakening effect upon the ventricles themselves. This is contrary to the usual teachings in regard to the effects and mechanism of the carotid sinus reflex, for the classic concept holds that the only cardiac effects are those which follow the inhibition of the pacemaker and that the vagus itself does not affect the ventricles directly. The available evidence has indicated that the response to carotid sinus stimulation is mainly mediated through the vagi and that sympathetic inhibition contributes only a small influence and then only after a latency of ten to fifteen seconds.6

It is commonly stated that stimulation of the carotid sinus or of the vagi directly produces bradycardia effects which are in accord with Starling’s law. Bazett7 states that following vagal stimulation, “the force of ventricular contraction is normally much increased owing to a greater filling resulting from a longer diastole.” This view, common to all texts of circulatory physiology read by this author, is based upon many observations of the augmented pulse pressures which occurs during vagal or carotid sinus stimulation in animal experiments. Recently Ring, Michie and Oppenheimer8 observed changes in the ballistocardiogram, electrolymogram and pulse pressure records following vagal stimulation of intact dogs. They found that in anesthetized dogs the period of prolonged filling was followed by a more forceful beat and thus concluded that the heart dilated and ejected more blood in accordance with Starling’s law.

Indeed Drury9 attempted to eliminate the complication of bradycardia during experiments designed to determine whether the vagus nerves had any direct action on the strength of contraction or refractory period of the ventricles. He prevented the slowing by driving the ventricles electrically during the period of vagal stimulation. In spite of the difficulty in interpreting Cushny myograph records and the abnormal concurrent stimulation of the ventricles, Drury concluded that the vagi had no effects upon the ventricles. It should be remembered that the vagus nerve trunk is composed of many afferent and efferent fibers and that certain fibers have different properties than others, hence data based upon stimulation of the total nerve trunks may be misleading. A recent publication10 contained evidence that three entirely different responses followed carotid sinus stimulation in different species of animals and with different anesthetic agents. Many previous experiments were performed with slow mercury manometers or with manometers sufficiently underdamped to produce overshooting of the pulse recording. There seems to be no indisputable evidence denying the possibility that certain fibers which course the vagi directly affect the ventricles and previously reported data of the type illustrated here, especially from man, is quite meager.

B. Reflexes from the Viscera. Another unexpected reflex response was seen following traction on the visceral mesentery (fig. 4). During traction on the colon there appeared an abrupt fall in systolic and pulse pressure which disappeared promptly on release. This effect could be repeated at will and it persisted for as long as 20 seconds, which was as long as the traction was maintained. The same blood pressure effects have also been seen following gall bladder distention. It is noteworthy that there was no change in the pulse rate during this period of apparent weakening of myocardial contraction.

Because of its rapidity of onset and disappearance this effect can hardly be due to reduced filling. Nor will a reduction of peripheral resistance explain it, for the slight reduction of diastolic pressure was accompanied by a far greater reduction of systolic pressure and this, together with a consideration of the contour of the pulse, indicates that diminution of peripheral resistance is absent or slight.

What was probably a similar reflex effect on the heart was noted by Starr,11 who observed a reduction in the magnitude of the ballistocardiogram complexes following distention of
the bile ducts by injecting fluids through a T-tube placed in the common duct at operation.

Comment. Thus several reflex responses have been demonstrated which depress the strength of cardiac contraction; in one case this is associated with a slowing of the pulse, while in the other it is mediated by a mechanism which has no influence upon the pacemaker. The results raise several fundamental questions. If vagal activity is solely responsible for the weakening effect, why is there not a bradycardia following mesenteric receptor stimulation as there is during carotid sinus stimulation? If the cardiac depression is induced by sympathetic inhibition why do these effects appear and disappear so rapidly? We are apparently dealing with a direct effect on ventricular muscles such as would occur if the responsible fibers entered the ventricles directly.

No classic concept will explain these phenomena. The results of the classic physiologic experiment in animals have been interpreted to mean that parasympathetic fibers have no direct effects upon the ventricle. Also, the response to changes of sympathetic activity occurs after a latent period, and the response persists for a time after such activity has ceased. But, as will be pointed out again, the evidence supporting the belief that vagal fibers do not penetrate the ventricles is not infallible, and, if sympathetic inhibition plays a role in the phenomenon we observe in man, such inhibition must occur far more rapidly and quantitatively in man than seems likely from the results secured in animals.

III. The Relationship of Pulse Rate to Other Cardiovascular Alterations.

Under this heading will be presented other data secured on man which seems inconsistent with the classic physiologic concepts. Marey's law states that the pulse rate is inversely proportional to arterial blood pressure. The common relationship found in animals, alterations of heart rate caused by changes in venous return and venous pressure, are attributed to the McDowell and Bainbridge reflexes. The following examples of the results secured in man are offered as evidence that none of these generalizations can be used to predict the pulse rate response in many situations found in the clinic. In addition to the well known pressure receptors in the great veins, pulmonary vasculature, carotid sinuses and aortic arch, there are receptors in the more distal part of the body which may exercise a dominating control over the pacemaker.

Results Obtained during Spinal Anesthesia. Figure 5 represents a response which was predictable on the basis of existing generalities. Following the administration of amyl nitrite the pulse pressure fell, the dicrotic notch disappeared and the pulse rate rose rapidly. A considerable amount of blood was pooled in the legs. The legs were then elevated; the blood pressure rose as the stroke volume increased and the pulse rate accordingly slowed. All this would be expected from our knowl-

![Fig. 4. Effect of traction or distension of the mesentery. Such traction produced an immediate drop in pulse pressure. Release of traction resulted in an immediate return to normal. No such effect occurred following traction on the colon after removal of the mesentery. This effect was not the result of any mechanical effect upon the large vessels in the abdominal cavity. This effect could be repeated at will.](image-url)
edge of classic physiology. Blood which accumulated in the legs because of vasodilation, increased the venous return when the legs were elevated.

pressure fell and his pulse rate increased. After a differential spinal anesthesia this procedure was repeated and then while his blood pressure fell as it had before, his pulse rate fell markedly.

![Figure 5](image-url)  
**Fig. 5.** Typical effects following administration of amyl nitrite in the supine position. Section A: At arrow amyl nitrite was inhaled. Note that the dicrotic notch drops out and the blood pressure begins to fall. Except for the period of eleven beats seen in the middle of this section the vertical segments indicate 1 second. Note the marked increase in respiratory variations of blood pressure. Section A1: At arrow the legs was elevated. Note the abrupt rise in pulse and mean blood pressure and the resulting slowing of the pulse rate.

Figure 6, on the other hand, demonstrates an entirely different response. In this case, during spinal anesthesia there were changes of arterial blood pressure which were quite similar to those following administration of amyl nitrite to the previous case; but, in the presence of spinal anesthesia, there was no acceleration of the heart. The patient reported absence of sensations below T-12 and the flushing and warmth of the lower limbs, measured by skin temperature, indicated pooling of blood in the extremities. Elevation of the legs produced an increase in stroke volume and blood pressure but again there was no change in heart rate. With anesthesia only to a level of T-12 we must presume that the nervous pathways from the aortic arch, carotid sinus and great veins were left intact. Nevertheless the usual pulse response was blocked. Evidently there are receptors and pathways mediated, in part at least, through the lower segments of the spinal cord which play an active role in the regulation of the heart's rate. In a previous publication1 a response was illustrated, but not described in detail, which demonstrates the complexity of these reflex pathways. A patient, who had had a sympathectomy from T-6 to L-3 for hypertension, was tilted to 70 degrees, the head being up, whereupon his blood pressure fell and his pulse rate increased. After a differential spinal anesthesia this procedure was repeated and then while his blood pressure fell as it had before, his pulse rate fell markedly.

![Figure 6](image-url)  
**Fig. 6.** These records demonstrate that, following spinal anesthesia to a sensory level of T-12, raising the legs above the level of the body while the patient is in the supine position causes a marked increase in pulse and blood pressure but no slowing of the pulse. The prolonged beats seen at the right of the upper 2 records result from speeding the recording paper. Except for these sections the vertical segments are 1 second apart. The hypotension following spinal anesthesia is, likewise, not followed by an acceleration of the pulse rate. Such a response has been noted following spinal anesthesia to a sensory level of T-10.
This observation has since been repeated in each of 6 patients tested.

To recapitulate: in the first case, after amyl nitrite the blood pressure fell and pulse rate rose. In the second, after a similar fall of blood pressure, pulse rate was unchanged. In the third, after a similar fall of blood pressure, pulse rate diminished. There was also a dissimilar response to an increase in blood pressure brought about by raising the legs. In these 3 cases the reflexes from the carotid sinus, aortic arch and great veins must be thought of as being intact. The difference of response must be attributed to differences in reflex mechanisms in the lower part of the body which thus seem either to facilitate normally or, under these conditions, to prevent the response associated with the receptors mentioned above.

Normally, tilting the head up results in well known changes. The pulse accelerates as the upright position is approached and when the proper correction for gravity is made it is found that the mean blood pressure at the level of the carotid sinus falls, that the pressure at the level of the aortic arch usually is unchanged and that the pressure below the aortic arch rises.12

Results Secured during the Valsalva Maneu-

ver. In a large series of subjects who performed the Valsalva maneuver it was found that there were individual variations in the degree of pulse rate and blood pressure responses; however, all normal unanesthetized subjects showed acceleration and deceleration of the pulse rate with decreases and increases in blood pressure. Figure 7 demonstrates this typical response and, in contrast, the response seen in each of 2 hyperthyroid patients tested. In the latter the pulse rate is completely uninfluenced by marked changes in blood pressure, which were doubtless accompanied by equally marked changes in venous return, cardiac output and peripheral resistance.

This difference in response in hyperthyroidism is perhaps comparable to results secured on animals. Rein13 stated that when vasodila-

![Fig. 7. Upper Record: Intra-arterial pressures obtained from a normal young man during the Valsalva experiment. At the arrow marked "blow 30 mm. Hg" the subject blew against a mercury column. At the arrow marked "Stop" this effort was relaxed. Lower Record: Records obtained by the same procedure in a hyperthyroid patient.](image)

![Fig. 8. Intra-arterial recording which is typical of the pulsus alternans seen so often following cyclopropane anesthesia.](image)

![Fig. 7. Upper Record: Intra-arterial pressures obtained from a normal young man during the Valsalva experiment. At the arrow marked "blow 30 mm. Hg" the subject blew against a mercury column. At the arrow marked "Stop" this effort was relaxed. Lower Record: Records obtained by the same procedure in a hyperthyroid patient.](image)

![Fig. 8. Intra-arterial recording which is typical of the pulsus alternans seen so often following cyclopropane anesthesia.](image)
stop this arrhythmia. During an operation of carotid sinus denervation there appeared a marked increase in extra systoles and tachycardia as shown figure 2. In Following the infiltration of the adventitia of the carotid vessels with procaine this irritability disappeared.

IV. Results Indicating a Direct Vagal Influence upon the Ventrices.

Data already presented in this communication have suggested that certain nerve fibers influence the ventricles directly without affecting the pacemaker. Certainly the effects recorded in these patients were not consistent with presently accepted characteristics of sympathetic activity. Therefore our data is in conflict with the generally accepted belief that the vagal branches do not innervate the ventricles and that the only parasympathetic action upon the ventricles is a result of an effect upon the sinus or A-V node. It is commonly taught that ectopic ventricular rhythms cannot be inhibited by reflex vagal stimulation, as can sinus or nodal arrhythmias, and Robb16 knows of no anatomic evidence clearly demonstrating or refuting vagal-ventricular innervation in man. There are, however, species variations and such anatomic evidence is quite difficult to obtain.

However, data are shown in this paper which support the view that certain vagal fibers do effect the ventricles directly. One of the subjects had a complete heart block in addition to, or as a result of, a hypersensitive carotid sinus. There was no history or clinical evidence of heart disease in a morphologic sense. The heart was not abnormally enlarged and there was no history of congestive failure. It can be seen from figure 2 that there was complete dissociation of the ventricles from the auricles and the electrocardiogram indicates that the foci of the ectopic rhythm were located below the A-V node.

Stimulation of the carotid sinus by pressure caused asystole of the ventricles yet, at the same time, auricular activity persisted at almost the previous rate.

This may be an unusual phenomenon, but there have been numerous reports in the literature17–22 concerned with an acceleration of the pulse rate following atropine administration during complete heart block; two of these are worthy of additional comment. Salley21 reported one “unusual” atropine effect on ventricular tachycardia following coronary thrombosis. Following administration of atropine the ventricular rate dropped to 30 thus uncovering a complete heart block. In view of Drury’s9 previous report, Salley concluded that atropine may have had a direct action upon the ventricles. Field, Barker and Alexander22 reported a case in which direct faradic stimulation of both vagi failed to influence the heart in any degree. A few days later, however, similar stimulation produced a slowing of the ventricular tachycardia. Messer and co-workers23 have mentioned some of the problems in interpreting data based upon the use of drugs.

In the case represented in figure 2, following the intravenous administration of 1.2 mg. of atropine, a marked prolongation in the diastolic period was not followed by the same degree of weakening as previously, yet the heart rate was not changed significantly.

A consideration of the data reported here and by others suggests that such results have been found frequently and that the only unusual feature is that they do not conform to expectations based upon the results obtained by Drury and others working on more or less isolated systems and upon anesthetized animals. In view of the results obtained on man, it seems unjustifiable to exclude the possibility of direct parasympathetic effects on the ventricles in man. This innervation may, however, vary functionally or anatomically from one person to another.

V. The Peripheral Aspect of Reflex Activity.

Weiss and Baker24 secured data obtained by Riva-Rocci measurements to indicate that, following carotid sinus stimulation, blood pressure returns to normal more rapidly than the pulse rate. This they interpreted as indicating that the slowing of the pulse is but one manifestation of this reflex and that it is less important than vasodilatation in controlling blood pressure.

The data presented here do not confirm this
hypothetical entirely. Except for one individual who had hypertension (see fig. 3), it can be seen that after the cessation of carotid sinus stimulation the return of the blood pressure to normal is accompanied by increased pulse pressure and so is mainly a consequence of cardiac action. The difference of response in the patient with hypertension may have been due to a depression of cardiac strength which persisted beyond the depression of cardiac rate. The slope of the pulse contours and the fact that the pressure during asystole levels off well above colloid osmotic pressure are effects not consistent with marked vasodilatation.

It can be seen from the pressure levels and pulse contours shown in figure 4 that stimulation of mesenteric receptors in man resulted in little if any peripheral vasodilatation, for the systolic pressure dropped markedly while diastolic pressure dropped only a small amount, so it is the change in systolic pressure which is chiefly accountable for the fall in mean pressure. Gammon and Bronk,29 in describing the activity of the pacinian corpuscles in the mesentery, and Heymans and co-workers,26 who also worked on this reflex, disagreed about the peripheral vascular effects following stimulation of these receptors. In their publications they did not concern themselves with cardiac effects. The difference in result may be due to the different species of animals and different anesthetic agents used by the 2 groups.

VII. General Considerations of Reflex Activity.

When one attempts to consider the significance of such observations as these and to cover the literature which exists concerning cardiovascular reflexes, it is impossible not to ask the same question that Heymans asked26: "Are all vessels provided with reflex propriosensitivity?"

The evidence is increasing that reflex effects on the heart can arise from many locations in the body. In addition to the well known carotid sinus, aortic arch and mesenteric receptors, reflex activity has been associated with the great veins, the right auricle, the pulmonary vasculature, the ventricles, and yet the list is by no means complete. Angina-like symptoms have been associated with biliary disease27; carotid sinus stimulation has produced21, 29 as well as relieved20, 31 such a pain. Vascular changes have been correlated with activity of the stomach.32

Hitherto, the expectations of clinicians have been largely based on physiologic data secured in experiments on anesthetized animals. Evidence has now been presented to show that, when certain of these reflexes are stimulated or modified by anesthesia, there are marked differences in the manner in which the cardiovascular system readjusts to changes within itself. Similar modification of reflex response doubtless occurs in conditions of disease, and certainly many manifestations of disease are unexplained by existing morphologic changes in the cardiovascular system. While one may doubt whether reflex imbalance can be considered the sole cause of any single cardiovascular derangement, an understanding of the physiologic changes found in disease requires a knowledge of the many reflex mechanisms concerned with cardiovascular adjustments. Abnormality of the adjustments may amplify, out of proportion, the effects of morphologic lesions themselves. Observers in the past have suggested that during rheumatic fever there is an alteration of vagal tone.33, 34 Stead,35 Richards36 and others have repeatedly emphasized the complexity of attempting to relate cardiac filling pressure and cardiac output. The inability to relate these factors with any consistency is encountered not only in disease but in many physiologic events. Undoubtedly reflex changes such as those demonstrated in this paper are concerned with the ability of the heart and circulation to adjust to the needs of the moment, and they must be thought of as playing an important part in the symptomology and pathogenesis of the many abnormalities of function so often found in disease of the heart and circulation.

**Summary**

1. Data including selected records of direct intra-arterial blood pressures and electrocardiograms secured from almost 1000 subjects are shown. These records have been obtained from
man during anesthesia, surgery, clinical disease, physiologic and pharmacologic experiments.

2. The records chosen for presentation were selected because they demonstrate the occurrence in man of cardiovascular reflex responses that are not generally recognized and are not explainable by existing concepts of reflex effect.

3. The stimulation or alteration of certain reflex areas has been seen to produce an apparent primary weakening of ventricular contraction (in some cases concurrent with the induction of bradycardia, and in others independent of changes in the pacemaker system of the heart) in addition to indicated alterations in stroke volume, cardiac filling and arterial pressure.

These changes follow modifications of reflex systems which are said to mediate their activity upon the heart through the vagus nerves. In addition the effects are not consistent with the presently accepted response of the sympathetic nervous system. These reflexes modify the manifestation of Starling’s law, but to say that Starling’s law does not hold in man is to deny the existence of reflex and humoral cardiovascular effects.

4. Spinal anesthesia to a sensory level of T-12 has abolished the classic response of the pulse rate following changes in stroke volume, cardiac filling and arterial pressure.

5. From the type of evidence listed in 3 and 4 it has been concluded that either there are certain fibers from the vagus nerves which enter the ventricles directly and produce an effect of weakened strength of contraction or that sympathetic inhibition occurs far more rapidly and quantitatively in man than has been supposed previously.

6. Some general considerations of the significance of alterations of reflex balance in man are attempted.

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