the form of an ellipse. In this case, when the elliptical base passes into the circular systolic form, the transverse and the longitudinal axes shorten while the antero-posterior diameter increases in length. On account of the oblique, spiral direction of many of the fibres, the apex is also seen to rotate somewhat to the left and forward, and the longitudinal axis approaches the vertical to the plane of the base. As regards the displacement of the heart as a whole, it is interesting to note that the apex is the stationary point, while the base is drawn toward it in proportion to the decrease in the longitudinal axis. The suspension of the heart from the large arteries should *a priori* make the base the relatively fixed point; its movement toward the apparently free apex is explained by the recoil of the blood as it is driven forcibly through the arterial ostia and by the elongation of the great vessels under the increased systolic pressure.

The effect of the contraction upon the cavities of the ventricles consists in a more or less extensive obliteration of their lumen. Examination of maximally contracted hearts after death shows, however, that this is not complete. On the left side the short, tubular chamber of the relaxed organ is reduced in systole to a mere stellate slit at the level of the papillary muscles, while above their summits this slit widens to an appreciable space of an irregular conical form (see Fig. 1343 above). In the right ventricle also, when the crescentic cavity is reduced to a mere slit by the approximation of the outer wall to the

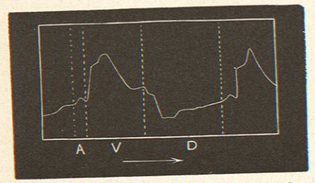

FIG. 1347.—Cardiogram Taken with Marey's Cardiograph. A, Auricular systole; V, ventricular systole; D, diastole. The arrow shows the direction in which the tracing is to be read.

septum, an appreciable opening is left in the upper part below the tricuspid valves, and more especially in the region of the conus arteriosus.

γ. The apex beat. At each systole of the ventricles a shock or impulse may be felt in the fourth or fifth intercostal space about an inch below and a little to the median side of the left nipple. This is where the apex lies against the chest wall uncovered by the lungs, and hence the name "apex beat" or "cardiac impulse" for this familiar phenomenon. In diastole the flaccid wall of the heart yields to the more rigid thorax and the apex is not perceptible to the touch. The sudden hardening of the ventricles as they contract upon their contents enables them to exert pressure against the chest wall so that now the apex can be felt distinctly, its contact with the thorax being made even closer by the forward rotation already referred to. The elevation of the chest thereby produced can be recorded graphically, and the tracings obtained are known as cardiograms.

The cardiogram gives valuable information as to the pressure and volume changes of the heart; its analysis will be attempted in connection with records of the heart's action taken by other methods. Special interest attaches to these curves from the fact that they represent the only direct record of the heart beat that can be obtained from man. (See the section on Cardiography in the article on *Heart*.)

δ. The heart sounds. Another physical sign by which the heart's action can be studied are the sounds which it emits. Normally two sounds, differing in pitch and duration, are audible in each cardiac cycle: the first a comparatively long, dull, booming sound, the second a short, sharp, sudden one. The interval between the first sound and the second is very short, but between the second and the succeeding first sound there is a distinct pause. The first sound is coincident with the systole of

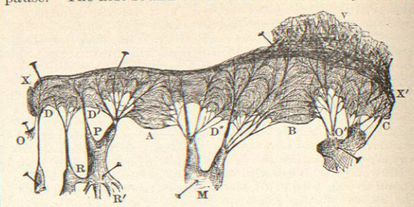

FIG. 1348.—Human Tricuspid Valve—Ventricular Surface Spread Out Flat. A, Inferior; B, anterior; C, septal segment; D D' D'', lesser segments; M, anterior papillary muscle; O O', papillary muscles attached directly to ventricular septum; P, papillary muscle attached to columnæ carneæ; R R' v, portion of right ventricular wall, showing bundles of fibres continuous with chordæ tendineæ; XX', line of insertion of segments into auriculo-ventricular ring.

the ventricles, more particularly with the closure of the auriculo-ventricular valves, and it is generally regarded as a mixed or combination tone in regard to its origin. It can be heard distinctly in a contracting heart containing neither blood nor air (Ludwig and Dogiel), so that it is partly at least a muscle tone. At the same time, it is probable that in the normally beating heart the sudden closure and tension of the auriculo-ventricular valves throw them and the blood into vibration, and it is possible that similar vibrations arise at the opening of the semilunar valves (Tigerstedt). The sounds resulting from these vibrations, by fusing with the principal element, the muscle sound, have some share in the total effect and thus help in determining its final character.

The second sound, which marks the end of systole, is purely valvular in origin, being produced by the closure of the semilunar valves. A sound exactly similar in quality can be obtained from the excised aorta by producing sudden tension of its valves. Considering the mode of production of the heart sounds, it is evident that each side of the heart must have a first and second sound of its own, making a total of four sounds. The fact that only two are ordinarily heard (the two first sounds fusing together and similarly the two second sounds) proves again the perfect synchronism of the ventricular contractions. Pathological alterations affecting either the structure of the valves or of the cardiac muscle may dissociate the elements of the mixed sounds, modifying

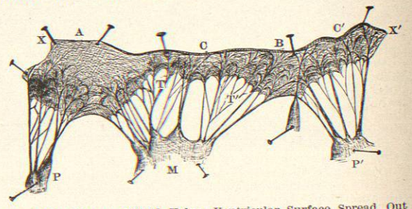

FIG. 1349.—Human Mitral Valve—Ventricular Surface Spread Out Flat. A, Largest cusp close to aortic valve, aortic segment; B, next largest cusp, parietal segment; C C', lesser cusps; M, anterior papillary muscle; P P', posterior papillary muscles; T T', method of branching of chordæ tendineæ; XX', line of insertion of cusps into auriculo-ventricular ring.

their usual character and quality and even giving rise to new ones. These abnormal sounds are known as cardiac murmurs, and from a study of their rhythm, their posi-

tion of maximal intensity, and the direction in which they are propagated information of great diagnostic value is obtained.

2. Internal Events of the Beat. α. During diastole, when the whole heart is at rest and its chambers relaxed, the semilunar valves are closed by the high pressure in the arteries. The blood, returning in the veins with a fair velocity and under low pressure, meets with no resistance and enters freely into the auricles, and thence passes onward into the ventricles. The auriculo-ventricular valves at this time are thrown open by the blood stream, but their cusps are more or less approximated by the eddies which return along the walls of the ventricles and carry the blood between them and the valve flaps. Presently the systole begins in the ends of the veins and with a sharp, short stroke passes quickly over the auricles. Without completely emptying themselves, they drive part of their contents into the ventricles where the pressure is lower than in the veins, and thus complete the filling of those chambers. The same reflux currents which previously floated up the cusps continue for an instant after the flow into the ventricles has ceased, and thus the edges of the valves are brought into apposition even before the ventricular systole begins. Their perfect closure is facilitated by the anatomical arrangement of the papillary muscles and chordæ tendineæ.

Each auriculo-ventricular valve may be regarded as a membranous tube attached to the auriculo-ventricular ring by one end along its whole circumference while the other end is deeply incised so as to form a number of separate flaps. These are attached to the inner surface of the ventricle and papillary muscles by tendinous chords arising not only from their free edges but also from their under surfaces. Each flap, moreover, sends its chordæ to more than one papillary muscle, and each of these in turn is attached to more than one valve flap.

As the systole of the ventricles begins and the pressure on their contents increases there is no regurgitation into the auricles. The pressure only more firmly secures the apposition of the thin free edges of the valves, and as they are put under tension the first sound is heard. The chordæ tendineæ prevent the eversion or even the bulging of the valves into the auricles, while the papillary muscles, contracting along with the rest of the heart muscle, serve to take in any slack in the chordæ which might result from the approximation of the base and apex, and so keep them taut. An accessory factor in the closure and support of the valves which deserves mention is found in the reduction in size of the base of the heart during systole with its consequent narrowing of the auriculo-ventricular apertures.

The pressure continues to rise in the ventricles until it exceeds that in the arteries, when the semilunar valves open and the discharge begins. The pressure on the arterial side of these valves being always considerable, their opening must not be thought of as a sudden bursting open with the separate folds thrown against the sides of the artery, but rather as a gentle yielding as the pressure on the ventricular side gains the upper hand. The free edges of the valvular folds are considerably removed from the walls of the sinuses of Valsalva, and this taken in connection with the thick projecting muscular cushions at the arterial apertures, reduces the opening through which the blood is discharged to a somewhat narrow slit. Eddies and whirls are formed in the wider space beyond, constantly tending to bring the valves together, and the moment the outflow from the ventricle ceases they close with such rapidity that no regurgitation occurs and the second sound is produced. The ventricle once more relaxes, the auriculo-ventricular valves open under pressure from the auricular side, and the whole cycle of events is repeated.

β. Intracardiac pressures. A record of the pressure changes in the several heart cavities during the course of a complete cardiac cycle gives the truest account of the force- and suction-pump action of the organ, and valuable hints for the determination of the time relations of the successive events which go to make such a cycle. Many methods have been devised to obtain such a record, and while the curves differ considerably in some respects, certain general conclusions have been obtained from them. In the first place, the upper and lower limits of the pressure reached in the course of an observation extending over a series of beats can be accurately measured by means of a mercury manometer with valves attached so as to convert it into a maximum or minimum manometer (Goltz and Gaule). This method shows that the maximum pressure in the ventricles is distinctly greater than the mean pressure in the corresponding arteries, that of the left ventricle being about 2.5 times as great as that of the right. In an actual experiment De Jaeger found the maximum pressure in the left ventricle of the dog 200 mm. Hg, and in another case Fick found it 160 mm. The pressure in the auricles is considerably lower, the maximum as measured on the right side being usually given at 20 mm. Hg. The minimum pressures in the cavities of the heart may fall below that of the atmosphere. Thus, in the left ventricle of the dog, it varied from —52 to —20 mm. Hg, in the right ventricle it was —17 mm. Hg, and in the right auricle —13 to —7 mm. Hg. Such values, however, are obtained only when the chest is closed, and the negative pressure of the thorax is partly responsible for these low pressures.

When the heart was exposed and the pericardium opened the lowest pressure in the left ventricle was —7 to —25 mm. Hg, and in the right, —1 to —2 mm. Hg, according to Goltz and Gaule. This observation has been con-

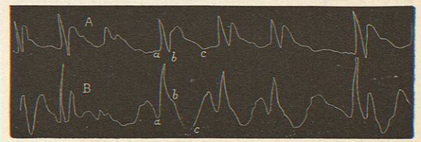

FIG. 1350.—Showing Curves of Pressure (A) and Velocity (B) in the Coronary Artery of the Horse. (Chauveau and Rebatel.)

firmed and denied repeatedly, but the balance of evidence seems to favor the view that the diastolic expansion of the heart walls may in itself produce a certain amount of suction, depending largely on the force and suddenness of the foregoing systole. Various suggestions have been made to account for it.

An elastic expansion of the ventricular walls has been assumed in this connection by some, but the evidence is all opposed to this view. A more efficient cause is probably to be found in the passive expansion which results from the peculiar conditions surrounding the coronary circulation. The filling of the blood-vessels in the walls of the heart should open up its cavities much in the same way that a double-walled bag is distended by filling the space between the two layers. Brücke's theory of the "Selbststeuerung des Herzens" was, in fact, based on this sort of mechanism. It assumed that the semilunar valves were thrown back during systole far enough to prevent the entrance of blood into the coronary arteries, whose distention at that time would oppose the systole; but when, at the onset of diastole, the coronaries are opened and the blood enters under strong pressure from the aorta, the diastolic expansion would be materially assisted. This theory has since been shown to be a curious mixture of truth and error. Martin and Sedgwick[9] demonstrated that the pulse in the coronaries was synchronous with that in other systemic arteries; therefore Brücke was wrong so far as the mechanism by which the systolic dilatation of the coronary vessels is prevented is concerned. The semilunar valves do not shut up the orifices of these arteries. Measurements of the velocity of the blood flow in the coronary arteries by Chauveau and Rebatel have shown, on the other hand, that he was right as to the facts.[10]

Their curves (see Fig. 1350) show that the tension and

rate of flow both increase in the coronary artery at the beginning of systole (*a*): *i.e.*, blood streams into it at this time. Then a second rise of pressure is observed during which, however, the velocity curve drops below the abscissa (*b*). This is the moment when the contraction of the ventricle becomes powerful enough to compress the intramural vessels and squeeze out their contents; hence the rise of pressure and the reversed current in the main vessel. Lastly, a new acceleration of the rate, not accompanied by a rise of pressure, appears (*c*); the diastole has begun, the vessels are once more free, and the flow of blood through them is re-established.

Porter[11] has recently added new testimony on this point in the form of observations on the outflow from the coronary veins during different phases of the heart's action. Among other results he found that the volume of blood passing through the coronary vessels is increased by an increase in either the force or the frequency of the heart beat, the increase of volume being accomplished largely through the periodical emptying of the intramural vessels by the systolic squeeze of the fibres around them. Some other points of interest concerning the coronary circulation may be briefly mentioned in this connection. The old controversy as to the terminal character of the arteries of the heart has been answered in the affirmative

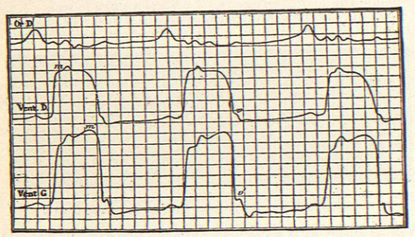

FIG. 1351.—Endocardiac Pressure Curves from the Horse. Or.D, Right auricle; Vent.D, right ventricle; Vent.G, left ventricle. (According to Chauveau and Marey.)

by the recent work from the Harvard laboratory. It was shown that ligature of the individual branches results in infarction and necrosis of circumscribed areas corresponding to the distribution of those branches. The effect of such a ligature on the action of the heart as a whole seems to depend entirely on the extent of the area involved, arrest of the heart following ligature of the R. circumflexus in 64 per cent. of the cases; of the R. descendens in 28 per cent.; of the R. septi in 0 per cent., and of the A. coronaria dextra in 14 per cent.

The old theory of a localized coordinating centre upon which the maintenance of the normal beat depends can no longer be defended in the face of these results. Finally the relation between the volume of the coronary circulation and the rhythmic contractility of heart muscle has been investigated by means of an artificial circulation, the applicability of which to the hearts of warm-blooded animals was demonstrated by Martin.[12] The work shows that a surprisingly small flow suffices to maintain a rhythmic beat, the ordinary volume used in the experiments of McGrath and Kennedy[13] upon vigorous cat hearts ranging from 3.5 to 13.5 c.c. per minute. Variations in the amount of blood fed to the heart influenced the force of the beats, while the rate was but little affected.

To return to the subject of intracardiac pressures, the oscillations between the limits given above must recur in the course of every cycle, and the rate at which the changes of pressure are made must be quite swift. It has been estimated that the pressure within the left ventricle rises at the rate of more than 2,000 mm. Hg per second. To obtain an exact record of such a change calls for an instrument with a quick response and low inertia; but the records obtained with the most improved spring manometers of recent years agree so nearly with the older curves of Chauveau and Marey in all essential points that we may assume for the present the correctness of their curves.

The auricular curve shows a quick, sudden rise of pressure which reaches its maximum in about 0.1 second, but returns again immediately so as to form a single rounded peak. This agrees exactly with the sudden brief systole of this end of the heart.

The steep rise of the two lower curves (Fig. 1351) shows that the ventricular systole follows immediately upon that of the auricles and that the pressure goes up with great rapidity. Then there follows a portion of the curves which goes by the name of the "ventricular plateau" because it extends in a direction more or less parallel to the abscissa, sometimes rising, sometimes falling a little, according to the method used. It represents graphically the maintenance in contraction of the ventricles, their systole lasting about 0.4 second. The lever finally sinks back abruptly to the base line and beyond, as shown in the descending limb of the curve.

Intraventricular pressure curves always present secondary elevations distributed over the main curve. They are not constant as to number or form, seemingly changing with the kind of instrument used, and some of them are unquestionably artefacts. Others correspond to definite processes going on inside the heart, as, for example, the small wave which is nearly always seen preceding the large rise due to the ventricular systole. Its position shows that it is synchronous with the systole of the auricle, the effect of which on the pressure in the ventricle is thus recorded.

There is no indication on the record either of the closure of the auriculo-ventricular valves or of the opening of the semilunar valves. An appreciable time must elapse after the beginning of the systole before the pressure mounts high enough to force open the semilunar valves against the arterial pressure; but this being a gradual process, as we have already stated, an effect in the form of a break or notch upon the curve would hardly be expected. By taking simultaneous records of the pressure in the left ventricle and in the aorta it has been shown that the pressure in the latter begins to rise about 0.1 second later than in the ventricle. The point on the curve which corresponds to the time of opening of the valves must be situated, therefore, near the top of the ascending limb and is not marked in any way.

The same indirect method must be relied on to determine, upon the curve, the position corresponding to the closure of the semilunar valves. They will close, of course, the instant the pressure within the ventricle falls below that in the artery, and upon the curve must be represented high up on the descending limb not far from the beginning of the steep descent from the plateau. The curve again shows no record of this event.

γ. The duration of the component elements of a complete cardiac cycle is found most accurately from such records as have just been described. For the human heart, however, it must be estimated from observations on the heart sounds and from cardiographic and sphygmographic curves.

Leaving out of account the slight differences in the figures as given by various observers, the duration of the phases of the human heart, beating at the rate of 70 per minute, may be stated as follows:

Ventricular systole	0.379	second.
Ventricular diastole	.483	"
	.862	"
Auricular systole	0.1	second.
Auricular diastole	.762	"
	.862	"

The heart pause in this case equals 0.383 second. The power of rapid recuperation of the musculature of the

heart is impressively shown by these figures. Another point of fundamental importance should be noted in this connection. It will be shown later that the rate of the heart varies within wide limits at different times and under different conditions; but throughout these extensive variations the duration of the ventricular systole remains remarkably uniform. In man, for example, it has been found that the ventricular systole varied only between 0.382 second and 0.190 second when the pulse rate ranged from 32 to 124 per minute. The variations in the rate of the heart are essentially dependent on changes in the duration of the pause, while the systole is but slightly affected. Even the pressure in the arteries has been shown to have no appreciable influence on the duration of the systole, the heart apparently possessing in a high degree the power of adapting its work to the varying demands made upon it without loss of time.

δ. The work done by the heart. In considering the work of the heart, it is treated practically as a force pump which discharges a certain volume of liquid with a known velocity against a given resistance. The auricles from this standpoint become unessential attachments to the apparatus, although physiologically they may be important enough. They not only provide reservoirs for the reception of the blood during the relatively long ventricular systole, thereby avoiding stagnation or damming back in the veins, but, as we shall see later, they constitute a regulating mechanism for the work of the ventricles by determining both the rate of their beat and the extent of their charge.

The suction of the ventricles already explained is here also disregarded. This suction, together with that of the thorax as a whole, is favorable to the circulation in that it assists the return of the blood in the veins. It may be neglected at present as it is quite insignificant in comparison with the other factor concerned, and the blood would return to the heart without its aid under the influence of the impulse given to it by the heart at the arterial end.

The work done by the heart is expended in two ways: (1) The contents of the ventricles must be discharged against a resistance measured by the mean pressure in the aorta and pulmonary arteries. Taking the left side alone for the present, work will be done at each beat equal to P × R, P being the "pulse volume" or the amount discharged in a single systole and R the mean blood pressure in the aorta. (2) Work is done in conferring upon the blood discharged a certain velocity. Now the kinetic energy represented by a mass in motion is expressed by the formula $\frac{1}{2}mv^2$, which if m equals the weight of a body under the influence of gravity, may be written $\frac{pv^2}{2g}$. Applied to the heart, p in this formula represents again the pulse volume, v the velocity in the aorta, and g the accelerating force of gravity, *i.e.*, 9.8 m. (32 feet). The total work of the left ventricle, therefore, equals $PR + \frac{Pv^2}{2g}$ and can be calculated if we know the pulse volume of the heart, the mean aortic pressure, and the rate of flow in the aorta. The two latter have been determined with a fair degree of approximation and may be taken at 150 mm. Hg for the pressure and 500 mm. per second for the velocity. Neither of these figures is very exact, but the error introduced by inaccuracies in them has little effect on the result as compared with that due to our ignorance of the pulse volume. An exact determination of the latter would furnish the key to many problems in the mechanics of the circulation, and frequent attempts have been made to get at it. The estimates given for the human heart vary all the way from 45 to 188 gm.; for the present 100 gm. may be taken as a fair average, although the true result will probably be found somewhat less than this.

Substituting the given values in the formula and making the correction for the specific gravity of mercury (13.6), we obtain as the work of the left ventricle:

$$w = 100 \times 0.150 \times 13.6 + \frac{100 \times 0.500^2}{2 \times 9.8}$$

or $w = 204 + 1.28$ gm.-metres of work.

The calculation for the right ventricle is made in the same way, the pulse volume of the two sides of the heart being assumed to be equal and the mean pressure in the pulmonary arteries being taken at $\frac{2}{9}$ that in the aorta. The work of the right ventricle is therefore equal practically to $\frac{2}{9}$ of 205.28, or 82.11 gm.-metres.

Multiplying the work of both sides (287.39 gm.-metres) by the number of beats per minute (70) and by the number of minutes in twenty-four hours (1,440), the work of the heart done in one day is found to equal 28,969 kgm.-metres as a conservative estimate. This represents a considerable percentage of the total energy production in the body, when it is remembered that the mechanical work done by a man in eight hours is estimated at about 125,000 kgm.-metres and that of the muscles of respiration in twenty-four hours amounts only to 11,700 kgm.-metres.

ε. The rate of the heart. It is a matter of some practical importance to the physician to know the normal rate of beat of the heart, and on this account numerous statistics have been compiled with the view of determining the relative influence of the various conditions and circumstances which affect it. Ordinarily the pulse rate presents more or less regular and extensive variations in the course of a day, which are sometimes designated "diurnal." They are hardly the expression of an inherent rhythmicity, since they almost disappear when the subject rests quietly in bed and abstains from food and drink, but rather the result of the complex and ever-changing activities which characterize the successive periods of a complete day.

The most potent of these physiological factors which affect the heart rate in any given individual are temperature and exercise. Experiments on the isolated mammalian heart[14] have shown that the rate increases with rise of temperature up to about 41° C. Beyond this optimum point, a further rise of temperature becomes harmful and quickly the lethal point is reached (45° C.). A change of temperature may arise from internal causes, as in fevers with their characteristically accelerated pulse, or it may come from external sources, such as the ingestion of hot or cold substances. The latter fact accounts in part for the distinct rise in the daily temperature curve after meals, although the quickened pulse at those times may be due partly to the increased chemical and muscular activity of the alimentary tract.

The effect upon the pulse rate of muscular exercise, which is familiar to every one, is both sudden and marked, and it may almost be stated as a law that the increase in the rate is proportional to the duration and intensity of the work done. On this account the pulse is slow during sleep, when the minimum is usually reached, and the increase in rate on sitting up or standing over that of the recumbent position is probably the result of the muscular efforts involved in maintaining these upright positions. The effect of exercise may be quite transient or it may persist for a considerable time, depending on the length of the previous exertion. Thus a walk of a mile or two at an ordinary moderate gait will keep the pulse rate quickened for thirty or even sixty minutes thereafter, and this long-lasting after-effect must be taken into account whenever observations on the normal rate are to be made.

Extensive data in which accidental variations from the preceding causes were guarded against have been tabulated in order to determine the influence of sex, age, and size upon the rate of the heart. The conclusions so far reached may be briefly summarized as follows:

Age.—The average pulse rate is highest the first year after birth, being given at 134 per minute in one series of observations; it sinks steadily up to the twenty-first year when a rate of 72 is reached; it remains at this level to about the sixty-fifth year, after which it begins to go up again slightly, rising perhaps to 79 or 80 per minute at the eightieth year.

Size.—The differences just noted depend in large meas-

ure on differences in size, although age in itself, apart from size, has some influence. Taking the average of a great number of cases, there is no doubt that tall individuals have a slower heart than smaller ones of the same age, the difference being as much as 23 beats per minute in the first year, but sinking into insignificance later on in life.

Sex.—Comparing males and females of the same age, the pulse rate is found to be more rapid in the latter at all ages from the second year on. Women on the average are a little smaller than men, so that a correction for size should be introduced. Even when this has been done the general statement remains true, although the differences then are smaller than they ordinarily appear.

The following tables, abridged from those given by Volkmann, furnish the basis of the foregoing generalizations:

TABLE I.

Age.	Heart Rate.			Number of observations.
	Maximum.	Minimum.	Average.	
0– 1	160	101	134	59
5– 6	128	70	98	56
10–11	106	56	87	73
15–16	112	66	83	77
20–21	99	59	71	67
30–35	104	58	70	125
40–45	104	50	72	105
50–55	94	52	72	42
60–65	100	54	73	60
70–75	104	54	75	44
80+	98	63	79	31

TABLE II.*

Age.	Mean Pulse Rate.	
	Male.	Female.
2– 7	97	98
8–14	84	94
14–21	76	82
21–28	73	86
28–35	70	78
35–42	68	78
42–49	70	77
49–56	67	76

* The average rates in this table were obtained by Guy from twenty-five observations, in each case taken at midday upon fasting individuals who were at rest in a sitting position.

TABLE III.

Height in millimetres.	Mean Pulse Rate.	
	Male.	Female.
525	158	144
875	110	107
975	101	106
1,075	97	98
1,175	91	94
1,275	88	95
1,375	87	87
1,475	85	84
1,575	75	77

From a teleological point of view the correlation between the pulse rate and the conditions enumerated above is easily understood. It provides an arrangement for adapting the circulation to the intensity of general metabolism through the rate of the heart. The smaller the size of the body, the greater will be the ratio of the surface to the mass and hence the more rapid the heat dissipation; hence to keep up body temperature heat production must be raised in the same proportion, *i.e.*, greater metabolic activity is required which in turn demands a more rapid circulation and a faster heart. In the same way the chemical activity of the muscles is heightened by exercise and again the circulation is accelerated. The exact mechanism by which the quickened pulse is obtained is difficult to determine, being in most cases of a complex character. The effect is sometimes a direct one on the heart itself, effected through the altered physical and chemical conditions of the blood; at other times it is mainly produced indirectly through the nervous system by way of the extrinsic nerves of the heart; usually it is the combined result of various interacting factors.

III. The Regulation and Adaptation of the Vascular Mechanism.—A rigid circulatory system working with the regularity of a dead model and supplying each organ with the same steady stream of blood, irrespective of its needs, would by its very regularity work its own destruction. In a living organism there must be a continual adjustment in the blood supply to each part with every change in external or internal conditions. The regulating mechanism, as we actually find it, comprises two parts: one connected with the heart, which being central produces general effects only; the other with the peripheral blood-vessels, through which both local and general effects can be brought about. As usual, the coordination and regulation of the blood vascular system are obtained through the mediation of the nervous system, the relation of which to the heart and blood-vessels must now be described.

A. *The Innervation of the Heart.*—It is customary to speak of the nerve supply of the heart as consisting of an extrinsic and an intrinsic mechanism. The extrinsic nerves include efferent fibres, which are supplied by the vagi and the cardiac rami of the sympathetic chain, and which approach the heart at its venous end, and afferent fibres, which pass from the heart at its arterial end and are characterized by their larger size and the presence of the medullary sheath.

In the mammal the extrinsic nerves terminate in plexuses around the arch of the aorta, and from these the intrinsic nerve supply is derived. Branches proceed to the junction of the great veins with the heart to be distributed to the various parts of the organ. Ganglia are abundant on the superior vena cava and are found also on the pulmonary veins, in the walls of the auricles, in the auriculo-ventricular groove and for an undetermined distance down the ventricular walls. Both nerves and ganglia lie for the most part superficially under the pericardium, and as they are traced along the heart from the point of entrance it may be said in general that the proportion of medullated to non-medullated fibres goes on decreasing, and that the number of ganglion cells likewise diminishes, disappearing entirely at or near the apex.

The ganglia are often classified as sinus ganglia and auriculo-ventricular ganglia. This separation into groups is obscure in mammals, but in the frog's heart comes out distinctly, the sinus ganglion located at the junction of sinus venosus and auricles being known as the ganglion of Remak, the auriculo-ventricular ones as the ganglia of Bidder.

In the frog the vagus and sympathetic fibres reach the heart in a common trunk, one on each side, passing along the superior cavæ to the ganglion of Remak. From this, in addition to scattered fibres, two main cords, the anterior and posterior septal nerves, proceed to the ganglia of Bidder. From the latter smaller twigs penetrate the substance of the ventricle, scattered nerve cells occurring for some little distance along their path; but the lower part of the ventricle, perhaps the lower two-thirds, is said to be quite free from them.

1. The Development of the Normal Beat. In order to appreciate the part played by the nervous apparatus of the heart, it will be necessary to consider the mode of development of its normal beat, of which the automaticity, the rhythmicity, and the regular sequence of the several chambers constitute the most striking features.

α. Automaticity. It has long been known that the heart of a cold-blooded animal will continue to beat for hours and even days after it has been removed from the body. There was every reason to think that the mechanism by which the beat is developed is the same in all the

vertebrates, and much of the physiology of the heart as worked out on the frog was applied to the mammal. More recently H. Newall Martin[12] succeeded in keeping alive the isolated heart of the latter also by supplying it with a suitable artificial circulation, and the question of its automaticity was definitively settled. The nerves reaching the heart from without were evidently not essential to the beat, for which all the conditions were contained within the organ itself. The heart is an automatic organ whose activity depends on some internal stimulus, and the question as to the nature of this stimulus and its point of attack immediately arises. Two answers have been given and are still current in physiology under the names of the "neurogenic" and the myogonic theories of the genesis of the heart beat.

The neurogenic theory is based on the following considerations: Muscular tissue in general, and especially the more highly differentiated types of it, depends upon its motor-nerve impulses to set it into action, whereas nerve cells constitute the automatic tissue of the body par excellence. Assuming similarity of function or properties in all nerve cells, those within the heart included, an easy explanation of the automatic beat of this organ would be furnished by the rhythmic motor impulses sent to the cardiac muscle by its intrinsic ganglion cells. Those who adopt this view urge in its support the interesting correlation between the number of ganglion cells distributed to each segment of the heart and the degree of spontaneity and rhythmicity which that part possesses. Thus upon the frog's heart, in which the normal beat begins in the large veins leading to the heart and sweeps over the sinus venosus, auricles, ventricle, and bulbus arteriosus in regular sequence, the following observations can be easily verified.

When the heart in dying ceases to beat the several segments come to rest in turn, beginning at the arterial end. The ventricle fails first, then the auricles fail, and lastly the sinus venosus fails. Further, on testing the irritability of the quiescent heart from time to time by means of gentle mechanical stimulation, its eventual disappearance is found to follow the same order as the failure of the natural beat. Lastly, if by means of a series of transverse sections carried through the heart at different levels the ventricular apex alone, or the entire ventricle, or the ventricle with some auricular tissue, be in turn separated from the venous end of the heart, it will be found that the sinus venosus possesses the greatest potentiality to beat, that the power of generating rhythmic spontaneous beats diminishes in the isolated piece as the plane of section approaches the apex, and that the apex itself will not beat spontaneously at all. The several segments of the frog's heart form, as regards their irritability and spontaneity, a descending series: sinus venosus, auricles, entire ventricle, lower third of ventricle—very similar to the series they form when arranged with reference to the number of contained nerve cells. The inference that the rhythmic beat is the result of the activity of these nerve cells is natural and easy, and though based on observations upon the frog's heart it has been extended to the vertebrates generally.

The myogonic theory of the heart denies the immediate physiological connection between the ganglion cells and the development of the beat, and at present finds in them merely nutritive and distributing centres for the intrinsic nerve fibres, putting them on a level with the cells of the sympathetic and other peripheral ganglia rather than with those of the central nervous system. The origin and nature of the beat are referred entirely to the peculiar properties of cardiac muscle, and much evidence has accumulated in support of this view.

It is known in the first place that hearts or strips of heart muscle, entirely free from nerve cells, may under proper conditions pulsate rhythmically in a normal manner. Not to speak of the invertebrate heart, it is a familiar fact that the heart begins to beat in the fœtus long before any nerve cell appears in its vicinity, while a common laboratory experiment consists in suspending under slight tension a strip of the terrapin's ventricle and recording for hours its rhythmic contractions.

In the second place cardiac muscle does possess peculiar properties not found in other forms of muscular tissue, properties which seem to afford an adequate explanation of the rhythmicity of the heart, while its automaticity and normal sequence are at least as easily explained on the myogonic as on the neurogenic theory.

As to the causation of the beat on the myogonic theory, the suggestion has been made that the internal stimulus consists merely in the spontaneous dissociation of the contractile substance. Heart muscle is admitted to be less highly differentiated histologically than skeletal muscle, and may plausibly be assumed to have preserved in a greater degree the primitive and fundamental attributes of undifferentiated protoplasm. Its spontaneity would be an exhibition of the same property which is inherent in the amœba as well as in the ganglion cell and calls for no special explanation.

Another view has come to the front in the last decade, and the stimulus for the contractions of the heart is found again in the blood, as it was at the beginning of the century. The new idea developed in connection with the work on the nutrition of heart muscle. It was long contended that serum albumin is a necessary constituent of artificial nutritive media for the isolated heart, the proteid being added to the mixture directly or else supplied accidentally by the residue of blood and lymph adhering to the meshes of the heart wall. For this reason, it was maintained, isolated hearts could be kept beating on a physiological saline solution for a comparatively short time only. It was found, however, that a heart which had been completely run down on 0.6 per cent. NaCl solution would beat again for a time if a small amount of Na_2CO_3 was added, and when it had come to rest on this mixture, could be started up a second time by the addition of soluble calcium salts, giving a long series of strong and regular contractions. These remarkable observations were the beginning of a prolonged study of the action of the inorganic salts upon the heart, which is still in progress. One result of this work has been to direct attention to the high degree of tonicity possessed by heart muscle. In normal diastole the heart does not relax completely; it stops in a condition of permanent partial contraction, which constitutes its tone. This is obvious on comparing the normal diastole of a heart with the extreme relaxation of complete vagus inhibition or of death. The tone or tonicity of the heart, measured by the extent of its diastolic relaxation, was found to vary with the reaction of the medium and with the kind and amount of the inorganic salts present. Weak acids diminish, alkalies increase the tone, and a similar antagonism holds good between the potassium and calcium salts. The tone of the heart is, therefore, intimately dependent on the nutritive exchanges going on within its substance, and its diminution or loss may be an important factor in cases of dilatation of the heart. The subject of tonicity of the heart thus becomes a matter of practical importance from the standpoint of clinical medicine. Another result was the discovery of the special relation of the inorganic salts, particularly of calcium and potassium salts, to the causation of the beat[15 16]. Calcium not only diminishes relaxation and increases the tone, but it promotes contraction so that excess of this reagent brings the heart to a standstill in powerful systole. Potassium produces the opposite effect, and a normal rhythmic beat can be maintained only by preserving a proper ratio within comparatively narrow limits of these two classes of salts. From these and similar observations along the same line the conclusion has been reached that the beat of the heart in its normal relations in the body is the result of the interaction of the inorganic constituents of the blood with the heart muscle, the former providing the adequate stimulus, the latter the irritable agent whose complex living molecule responds to the stimulus with an explosive decomposition and furnishes the energy of the contraction.

β. Rhythmicity. On the assumption made in the fore-