THE PROGNOSTIC SIGNIFICANCE OF PULSE-PRESSURE CHANGES DURING HEMORRHAGE*

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Hemorrhage is a pathological process in which all organs suffer in function from the loss of blood, and the severity of the case depends not only on the quantity of blood lost, but also on the ability of the body to manage with that remaining. Consequently, our stock of facts for formulating a prognosis consists, first of all, of those data which indicate the degree that the body mechanisms are compensating and the extent to which the important functions are interfered with; and, in the second place, of those which indicate the progress of the bleeding itself. Thus the reaction of the higher nervous centers to the anemia is judged by the state of consciousness or stupor and the response of the corneal and pupillary reflexes, as well as the activities of the respiratory and cardio-inhibitory centers, as these are mirrored in the changed character of respiration and in the disturbances of cardiac rate and rhythm (Hayem,¹ Frédéricq.²) These signs, showing how well the body is enduring the hemorrhage, bear by no means a direct relation to the quantity of blood lost, nor to that remaining within the body, but, like immunity to infectious diseases, they vary, not only with race and species, but even in the same animal at different times.

Although the reactions of the body cells, many of them compensatory in character, are of great importance in prognosis and in indicating the management of the case, the prospects of ultimate recovery rest entirely on the probability of complete cessation of bleeding, for, obviously, the compensatory mechanisms cannot long remain active unless this occurs. But to a host of such questions as, "Has the hemorrhage ceased? Has it diminished, or has an exacerbation occurred?" the clinician can often supply no answer. This is owing, not only to the fact that hemorrhage

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* This investigation, the fourth in a series of studies in inaccessible internal hemorrhages, was carried out in the Physiological Laboratory of the University of Michigan.

1. Hayem: *Arch. de physiol. norm. et path.*, 1888, i, 106.

2. Frédéricq: *Travaux du Laboratoire de Liège*, 1885-1886; *Arch. de biol.* 1882, iii, 55.

is frequently associated with other pathological conditions (as for example, shock and infections), but as much to the fact that the results of experimental workers show very little relation between the signs and course of the bleeding. Thus, it has been established that the changes in height of blood-pressure, on account of the many interacting factors, bears no relation to the loss of blood (Worm-Müller,³ Dawson,⁴ Crile⁵). The same may be said of changes in heart-rate (Dawson⁴). A continued decrease in the percentage of hemoglobin or the number of red cells can also give no indication as to the course of bleeding, since both continue to decrease for several days after hemorrhage has ceased (Kiefer,⁶ Dawson,⁷ Crile⁵). This is particularly true in the case of large hemorrhages, in which a prompt diagnosis of the condition of hemorrhage becomes of the utmost importance.

It was with the hope that experimental methods might unearth some signs, which, by their changes, would offer a more rapid method of determining changes in the course of bleeding, that a series of experiments was carried out at the physiological laboratory at Ann Arbor, to determine the influence that hemorrhage or its cessation exerted on pulse pressure (that is, the difference between the systolic and diastolic pressures) and it seemed not unfitting to gather together the results, stripped as far as possible of technical details and adapted to trial in clinical cases.

This study of the behavior of the pulse-pressure during hemorrhage is preceded, to my knowledge, by only one other, that of Dawson,^{4, 8} who found (1) that, while both systolic and diastolic pressures fell during hemorrhage, either might be affected more than the other or they could be equally affected, and (2) that while pulse-pressure always showed a marked diminution which corresponded in direction with the change in systolic output, it bore no relation to the percentage loss of blood. No attempt has hitherto been made to utilize changes in pulse-pressure as criteria of the direction in which the course of a hemorrhage is trending.

THE SYSTOLIC OUTPUT OF THE HEART DURING HEMORRHAGE

Normally the volume of blood contained in the large veins and auricles is always somewhat in excess of the quantity that can be accommodated in the right ventricle during its next diastole. Since blood leaves the vas-

3. Worm-Müller: Ber. d. sassch. Gesellsch. der Wissensch., math. phys. Classe, 1873.

4. Dawson: Jour. Exper. Med., 1905, vii, 6.

5. Crile: Transfusion and Hemorrhage, 1909, New York, pp. 69, 100.

6. Kiefer: Med. News, London, 1892, ix, 225.

7. Dawson: Am. Jour. Physiol., 1900, iv, 1.

8. Dawson and Gorham: Jour. Exper. Med., 1908, x, 484.

cular system during hemorrhage, the quantity returned to the heart of necessity immediately diminishes, but, on account of the excess supply, the filling of the ventricle is not at once interfered with. Hence, a latent period, varying with the degree of bleeding from a few seconds to several minutes, intervenes between the beginning of hemorrhage and the time when the filling of the ventricle is effected (Fig. 1.) After this interval the ventricular filling becomes impaired, owing to the fact that the difference between the veno-auricular pressure and the pressure in the relaxing ventricle becomes less. The filling becomes more gradual during the period of active relaxation and extends into the period of diastasis, although the quantity injected by the auricles often remains practically un-reduced. Thus it comes about that the auricular contraction, which normally contributes so little to the ventricular filling, may acquire one-half of that responsibility (Fig. 2). The systolic discharge lessens

Fig. 1.—Effect of three hemorrhages and their cessation on the systolic output of the heart (upper curve) and the blood-pressure (lower curve). Heart-rate calculated from simultaneous record on faster drum.

during hemorrhage entirely as a result of this impaired filling. Even to the end, the nutrient supply of the heart is usually sufficient to enable it to carry on undiminished contractions. Incidentally, this observation shows that the fear, so often exhibited by physicians, lest the heart cease beating, is ungrounded, and that the administration of cardiac stimulants for this reason is quite unnecessary. As a matter of fact, the amplitude of contraction is often increased early in hemorrhage, causing the ventricles to empty themselves more completely.

When hemorrhage ceases, the supply of blood to the right heart increases with surprising rapidity. If hemorrhage stops suddenly, as in

the case of artificial hemostasis, the increase is immediate, owing probably to the increased arterial pressure which immediately follows the sudden occlusion of a bleeding vessel. If the occlusion occurs gradually through the natural process of clot formation, this influence is still felt, though to a diminished degree. In this case other compensatory mechanisms are chiefly responsible for the return of blood, these being the resorption of lymph by the capillaries and the modifying effect of the respiratory movements.

When the large veins are normally filled with an excess supply of blood, the act of inspiration may, by creating a negative pressure in the thorax, and by compressing the abdominal veins, favor the return of blood to the heart (de Jager⁹); but, according to Henderson,¹⁰ it is mechanically impossible for this extra quantity to be pumped out except by an increased rate of beat. I am able to confirm, I believe, that normally

Fig. 2.—Effect of hemorrhage on the rapidity of ventricular filling, taken on a rapid drum from same experiment as Figure 1.

the increase in heart-rate during inspiration is largely responsible for the augmented output per minute during that respiratory phase, but can not agree that respiration does not modify the filling of the ventricle. My records, as well as some of those published by Henderson, to my eye, indicate that the rate of ventricular filling during early diastole is less rapid in inspiration than in expiration. On account of the removal of the normal vagus tonus during hemorrhage, the respiratory variations in heart-rate are abolished and, therefore, the changes occurring as a result

9. De Jager: Arch. f. d. ges. Physiol., 1884, xxiii, 17; Jour. Physiol., 1886, vii, 194.

10. Henderson: Am. Jour. Physiol., 1906, xvi, 344.

of the intermittent quickening and slowing of the heart are absent. The variations which now take place in the systolic output are entirely to be accounted for by the altered filling during inspiration and expiration. The greater return of blood to the chest at the end of inspiration and the beginning of expiration results in a more prompt and complete filling of the ventricle during diastole (Fig. 3), the inflow becoming more rapid during the period of active relaxation, while the period of diastasis may be changed from one of gradual filling to one of practically no filling.

Fig. 3.—Showing more rapid and consequently more complete filling of ventricle during beginning of expiration. V. O., ventricular output; S, systole; D, diastole; P. P. pulse-pressure taken with a Hürthle manometer; R, respiration, the lever moving down in inspiration; T, time in seconds; X, relative position of writing levers.

When the duration and extent of hemorrhage become marked, this effect may be intensified by an augmentation and acceleration of the respiration. If expiration becomes forcible, the abdominal veins are compressed not only by the descent of the diaphragm in inspiration, but also by the

contraction of the abdominal muscles in expiration (Fig. 4). In all these ways respiration favors the return of blood to the large veins and auricles, and rhythmically augments the filling of the ventricles. This filling may furthermore be aided by a compensatory contraction of the auricle itself. Almost without fail, the filling of the ventricles and, in a corresponding measure, the systolic output are rapidly increased as soon as hemorrhage

Fig. 4.—Showing that forced expiration aids filling of ventricle. Lettering same as before.

ceases, as the compensatory mechanisms can now exert themselves without opposition. This never occurs so long as bleeding continues, for they are not able to overpower the effect of a continued drain of blood.

THE PULSE-PRESSURE AS AN INDEX OF SYSTOLIC OUTPUT

Having determined primarily that changes in the systolic output correspond with a fair degree of rapidity to changes in the course of a hemorrhage, the next query directed itself quite naturally to the question

of how accurately changes in systolic output were revealed by the pulse-pressure.

Dawson and Gordon⁸ recorded simultaneously tracings of the pulse-pressure and volume changes in the ventricles. Their tracings showed that under various conditions, hemorrhage included, a close correspondence occurred in their general course. They therefore concluded that the pulse-pressure might be taken as an index of the systolic discharge. Henderson, restudying the subject, pointed out, however, in his own data as well as in those submitted by Dawson and Gordon, that the pulse-pressure and systolic output bear a widely varying ratio to each other at different times, and hence he concluded that the pulse-pressure was not an accurate index of the systolic discharge.

In more than twenty experiments in which the pulse-pressure tracings taken by a Hürthle manometer were compared with the volume output of

Fig. 5.—Effect of large hemorrhage on pulse-pressure obtained from femoral. Lettering same as before.

the ventricles recorded from a cardiometer, in principle that of Henderson's, it was found that, in general, the two tracings followed each other so closely during a hemorrhage that by covering one it was possible to prophecy the course of the other. Consequently, it seems that the clinician who follows the pulse-pressure changes within short intervals of time (5 to 10 minutes) obtains a general idea from his observations as to whether the systolic output is increasing or decreasing. Henderson's criticism, however, holds true during hemorrhage, for the same pulse-pressure may, at different times, be accompanied by differing systolic discharges. Hence, the clinician is not warranted in assuming that, because the pulse-pressure is equal to that obtained at some other time, the sys-

tolic discharges were equal. The pulse-pressure is never a quantitative measure of the systolic output; but, *when compared to some immediately preceding observation, may generally be used as a qualitative indication of the direction in which the systolic discharge varies.*

Exceptions to this statement, however, must be recorded. In the case of a large hemorrhage, the diastolic pressure suddenly falls and causes an increase in pulse-pressure, although the systolic output actually decreases (Fig. 5). This is due to the sudden lowering of resistance which the rupture of a large vessel causes, for as shown by Hürthle,¹¹ the pulse-pressure increases with a decreased and decreases with an increased peripheral resistance. Careful statistical analysis of those curves in which pulse-pressure and cardiac output per beat follow in the same direction shows that, early after the inception of the bleeding, the pulse-pressure is larger in proportion to the systolic output than later, when

Fig. 6.—Respiratory variations in pulse-pressure during hemorrhage. Lettering same as before.

the hemorrhage tends to cease. This may be accounted for by the fact that, as hemorrhage proceeds, the peripheral resistance is raised, not only by a general vasoconstriction, but also by the formation of a clot over the wound. After the bleeding has entirely ceased, the pulse-pressure may again become proportionately larger, a fact probably to be explained by a lessening of the viscosity of the blood, which occurs when the plasma is repleted by absorbed lymph. While the pulse-pressure may thus be affected by the changes in peripheral resistance, this factor is not sufficiently pronounced to cause it to deviate in direction from the systolic

11. Hürthle: Arch. f. d. ges. Physiol., 1888, xliii, 433.

output, except when the hemorrhage is very large. Even in this case the comforting fact remains that this increase is very temporary and is soon replaced by a progressive decrease.

As a second exception it must be mentioned that augmented and forcible respirations will rhythmically cause a marked augmentation of the pulse-pressure, as recorded by a Hürthle manometer, a change that is due chiefly to a periodic increase of the systolic pressure (Fig. 6). In such cases an average of these pressures may probably be considered an output index comparable with systolic discharges, when no such marked variation occurs. When such a comparison is made, however, it is found that the average pulse-pressure often shows an increase when no corresponding increase in systolic output is found. Hence, augmentation of the pulse-pressure, as determined by clinical instruments, when accompanied by forcible expirations, loses its value as a criterion of the degree of bleeding, for, by such instruments, we can obtain only the average pulse-pressure. In the common method of estimating the systolic pressure by palpating for the return of the pulse at the wrist, the first few "rudimentary" waves (von Recklinghausen¹²) are missed by the palpating finger (Janeway¹³) and, accordingly, the pressure read is never the highest occurring during a respiratory phase, but probably approximates an average. Since the diastolic variations are not marked, they can, for that reason, probably be disregarded without detriment to the results. Subtraction of this diastolic pressure from the average systolic pressure evidently gives a result approximating an average pulse-pressure.

Summary.—A progressive decrease in pulse-pressure indicates a continuance of the hemorrhage. An increase may signify, (1) that hemorrhage continues, but that the effect of respiration has interfered with its true relation to the previous pulse-pressure; (2) that hemorrhage has ceased; or, (3) that it has become exacerbated. The existence of augmented respirations can be ascertained by observation, but the fact that the same change may indicate either a cessation or a great augmentation is, at first thought, not encouraging for establishing a prognosis. It is, however, possible to differentiate. An increase in pulse-pressure due to an augmentation of hemorrhage is temporary and is soon supplanted by a marked decrease, whereas an increase due to cessation of hemorrhage remains permanent at subsequent measurements. Furthermore, the heart becomes accelerated (unless already very rapid) if the hemorrhage has increased, whereas no such change accompanies a cessation.

12. Von Recklinghausen: *Arch. f. exper. Path. u. Pharmacol.*, 1901, xlv, 103.

13. Janeway: *The Clinical Study of Blood-Pressure*, 1904, p. 62.

THE MINUTE OUTPUT DURING HEMORRHAGE

Experimental investigations (Henderson¹⁹) have satisfactorily established that an acceleration of the heart may itself act to reduce mechanically the output of blood per beat. Since during hemorrhage the heart-rate increases, the question naturally arises, "How is it possible to determine whether the reduction of pulse-pressure is due to a loss of blood, or is a natural consequence of the cardiac acceleration?" A determination of the volume of blood discharged by the ventricle per minute, or the minute output, as it may concisely be styled, offers a means of differentiation. This systolic output per minute may, in the case of regularly beating hearts, be determined experimentally by multiplying the systolic output by the number of beats per minute. Since the pulse-pressure gives a qualitative indication of the changes in systolic output occurring in consecutive intervals, the variations in minute output may be followed by obtaining the product of the pulse-pressure and heart-rate. Henderson has shown, however, that if the acceleration of the heart is not too great, the minute output will always *increase as the heart-rate increases*. During hemorrhage the minute output, as estimated by the product of systolic discharge and heart-rate, *always decreases as the heart accelerates*. Consequently, the product of the pulse-pressure and heart-rate may also be expected to decrease as the heart-rate becomes more rapid. Experiments show this to be the case, except in the two instances before pointed out, in which the pulse-pressure was not changing in the same direction as the systolic output, that is, during markedly augmented respirations and at the beginning of very large hemorrhages. In these cases the product increases.

CONCLUSION

While there are interfering factors which may at times mask the significance of pulse-pressure changes, the deduction may be drawn that many cases of hemorrhage must occur in practice in which these pulse-pressure changes may be of value in following the course of bleeding.

The following series of procedures may then be recommended for following the course of a suspected or diagnosed internal hemorrhage:

1. Eliminate as far as possible psychical factors in the patient by the administration of the customary dose of morphin.
2. Determine the systolic and diastolic pressures by means of the sphygmomanometer at intervals of not more than ten minutes, and more frequently if possible. By subtraction obtain the pulse-pressure. Also determine the rate of the pulse and respiration.

3. Tabulate the data as the observations continue. If the respirations undergo little or no change, the following deductions may be drawn: A: A progressive decrease in pulse-pressure and decrease in the product of the pulse-pressure and the heart-rate indicate a continuance of the bleeding. B: An increase of both, if permanent, after several determinations, indicates a cessation of hemorrhage. C: A temporary increase of both, followed by a marked decrease on subsequent examinations, indicates an exacerbation.

If it is true, however, that such determinations possess a clinical value, the fact should be capable of demonstration in a similar manner on animals. I have not, as yet, had time to test my skill in following the course of a sufficient number of such hemorrhages to draw final conclusions, but the results incorporated in the table appended give an indication of the close correspondence in a number of cases. In these experiments hemorrhages were produced in dogs by an assistant, at intervals and times unknown to me. With maximal and minimal manometers I determined at various intervals the data, as outlined above, incorporated them in the table, made my predictions, and compared them with the actual state of hemorrhage. Since these experiments are so few in number, I shall refrain from remarks concerning them, except to state that they are suggestive of future possibilities.

TABLE OF PULSE-PRESSURE CHANGES IN CONNECTION WITH HEMORRHAGES
EXPERIMENT 369, FEB. 27, 1910

Time.	Heart Rate.	Systolic Pressure.	Diastolic Pressure.	Pulse Pressure	Minute Output.	Predicted Course of Hemorrhage.	Actual Course of Hemorrhage.
3:00	110	90	62	28	3080		
3:05	126	62	46	16	2016	Hemorrhage started.	Hemorrhage lasted
3:13	126	72	58	19	2394	Hemorrhage stopped.	3.03 to 3.06.
3:18	126	42	33	6	756	New hemorrhage.	Hemorrhage lasted
3:32	126	64	40	24	3024	Hemorrhage stopped.	3.15 to 3.19.
3:38	144	68	42	26	3744		
3:40	156	39	24	8	1248	Large hemorrhage.	Hemorrhage lasted
3:50	150	37	27	10	1500	Decreased?	3.38 to 3.41.
4:02	159	28	18	10	1500	Continued?	

EXPERIMENT 377, APRIL 12, 1910

Time.	Heart Rate.	Systolic Pressure.	Diastolic Pressure.	Pulse Pressure.	Minute Output*	Predicted Course of Hemorrhage.	Actual Course of Hemorrhage.
4:00	150	137	68	69	10350		
4:02	156	142	67	75	11700		
4:05	162	131	63	68	11016	Hem. started? Yes.	Hemorrhage lasted
4:10	162	124	63	61	9882		4.04 to 4.14½.
4:15	162	116	62	54	8748		
4:17	162	122	64	58	9399	Hemorrhage stopped.	
4:29	162	116	57	59	9458		
4:31	162	114	55	59	9458	Small hemorrhage?	
4:37	156	112	52	60	9360	No.	
4:39	162	94	50	44	7128	Exacerbation.	Hemorrhage lasted
5:01	162	78	44	34	5508	Continued.	4.37 to 4.40.
5:03	162	84	42	42	6809	Stopped.	
5:06	162	68	37	31	5022	Exacerbation.	Hemorrhage lasted
5:10	144	48	30	18	2892		5.06 to 5.10.

EXPERIMENT 378, APRIL 13, 1910

3:30	114	114	67	47	5358		
3:34	114	86	49	37	4218	Hemorrhage started.	Hemorrhage lasted
3:38	132	80	44	36	4752	Hemorrhage stopped.	3.30 to 3.34.
3:42	126	60	42	27	3402	Hemorrhage started.	Hemorrhage lasted
3:44	126	69	44	25	3150		3.38 to 3.39.
3:46	120	73	40	33	3960	Hemorrhage ceased.	
3:49	120	61	39	22	2640	Exacerbation.	Hemorrhage lasted
3:51	120	48	32	16	1920		3.39 to 3.46.

EXPERIMENT 379, APRIL 16, 1910

4:10	114	82	38	44	5016		
4:11	108	84	38	46	4968		
4:13	108	71	34	37	3906	Hem. in progress.	Hemorrhage lasted
4:14	108	72	36	36	3886		4.12 to 4.14.
4:16	108	73	36	37	3990	Hem. diminished.	
4:18	114	73	34	39	4446	Large exacerbation	Hemorrhage lasted
4:20	114	56	30	26	2964	Large hemorrhage.	4.18 to 4.21.
4:23	114	57	32	25	2350		

* Minute output estimated by product of pulse-pressure and heart-rate.

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