STUDIES IN CONGESTIVE HEART FAILURE: *II. The Respiratory Exchange During and After Exercise*

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STUDIES IN CONGESTIVE HEART FAILURE

II. The Respiratory Exchange During and After Exercise

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The first study of this series was concerned with edema, which is one of the two major symptoms of congestive heart failure. The other is dyspnea. If one carefully observes individuals with congestive cardiac failure he notes respiratory distress of at least three different types: (1) Paroxysmal dyspnea, which may occur when edema is present or absent; (2) continuous dyspnea at rest, which is rare except in those patients who have moderate or marked edema; (3) dyspnea on exertion, which may be observed in some degree in all individuals with congestive failure, and the presence of which is necessary for the diagnosis of congestive failure. Despite its constant presence in patients with "failing hearts," present knowledge of the underlying nature of dyspnea brought on by exertion in such individuals is far from complete.

In their important monograph, Eppinger, Kisch and Schwarz (1927) reported the results of an exhaustive study of cardiac failure. They found that the basal metabolic rate was often elevated, a finding which agreed with the results obtained by Peabody, Meyer and DuBois (1916) and by Mannaberg (1924). During the performance of a given amount of work the oxygen intake was usually within normal limits. However, after exercise the oxygen debt in many—not all—of their subjects was greater than in normal subjects and hence the total oxygen requirement was greater. The carbon dioxide production was relatively less than in normal subjects. The authors interpreted their findings as meaning that the buffering power of the body is diminished, due to lack of carbonate, and that the ability of the tissues to resyn-

thesize glycogen from lactic acid is impaired. Hence, more lactic acid is oxidized and the oxygen requirement is greater than in normal individuals.

Meakins and Long (1927) studied the oxygen intake during and after exercise in patients with mitral stenosis. They found that during a given exercise the oxygen intake was less in patients than in normal subjects. The maximum oxygen debt attainable was less and this they thought was due to the fear of the cardiac patient of driving himself too far. All of their subjects were suffering from rheumatic heart disease and chronic mitral endocarditis, and, judging from their protocols, their patients seem to have had little or no systemic congestion or edema.

Herbst (1928) compared the maximum oxygen intake of compensated cardiac patients with that of normal subjects when running at a rate of 280 steps per minute and found a considerable diminution in the former group who were only able to take in 1200 to 1800 cc. of oxygen per minute as compared with 1800 to 4000 cc. for the normals. He concluded that individuals with cardiac disease had an abnormally low maximal cardiac output per minute. He also studied compensated and decompensated individuals when doing work with their arms at the rate of 300 kilogram meters per minute. Numerous individual exceptions were noted but in general the decompensated patients exhibited greater rises in ventilation, lower oxygen intake during the exercise, larger values for oxygen debt and for requirement than did the compensated subjects. In Herbst's patients the basal metabolic rate was usually elevated but, since both the patients with and without congestive failure exhibited this phenomenon, he did not believe that the increase could be considered as a result of heart failure.

Because of the somewhat conflicting character of these observations our studies were undertaken.

METHOD

All observations were made in the post-absorptive state. Precautions were taken in order to make certain that the subjects should really be at their lowest metabolic level during the preliminary basal period. The normal subjects slept in the laboratory. The patients were wheeled in their beds to the laboratory one hour or more before the observations were begun. The subjects usually were

asleep until awakened when the operator adjusted the mask to their faces. After the mask (which was found to cause considerably less discomfort than a mouth piece and a nose clip) had been put on, a few minutes were allowed to elapse before the preliminary collection of air samples was begun. During this period and also after the exercise the subjects frequently "dozed" and in several instances actually slept. The position chosen was that in which the subjects felt most at ease. For the normal subjects and some of the patients, the recumbent posture was used. The head and shoulders of those subjects who suffered from orthopnea were propped up at whatever angle they desired by cranking up the head of the bed before the observations were begun.

With one exception the subjects were all trained to the method by preliminary procedures on previous days. The individuals who made the observations were the physicians in charge of the patients and were therefore well known to the latter, none of whom displayed anxiety or fear, although several patients were in extreme respiratory distress during and immediately after the exercise.

We have emphasized these details because they seem to us extremely important if one is to obtain actual *basal*—as distinguished from *resting*— metabolic rates. It appears that the low metabolic rates which we have found (see below) are to be explained by the measures which have been taken to insure physical and more particularly mental relaxation.

The expired air was collected in Douglas bags of various sizes. After samples had been taken volumes were measured by expelling the air into a 150-liter calibrated spirometer. The error of the volume measurement was not more than one per cent. The gas samples were analyzed in the Van Slyke-Neill apparatus (1924). We have modified their technique in certain respects, and the details will be published at a later date. According to the technique which we have used the average variation on duplicate oxygen determinations is about 0.08 per cent. The carbon dioxide error is somewhat higher, being 0.10 to 0.15 per cent Our values for oxygen consumption are therefore slightly less accurate and our values for carbon dioxide excretion considerably less accurate than if the Haldane apparatus had been used. For the purpose of this work the Van Slyke apparatus has seemed much more convenient and time-saving, and the additional error involved seemed not to invalidate the results.

After the basal period had been completed exercise was begun. Various types of exercise were used. In most of the observations which are reported here, the exercise consisted of walking 15 meters from the bed to a staircase (30 seconds), walking up the flight of stairs which consisted of 21 steps and a total height of 3.8 meters (40 seconds), turning and descending the stairs (40 seconds), and walking back to bed (30 seconds). An attempt was made to keep the time constant for each part of the exercise but minor variations occurred. As soon as the subject reached the bed a tap was turned and the expired air was shunted from the "exercise" bag into a larger "debt" bag. The duration of the after-period during which the expired air was collected was 20 minutes. In some experiments the expired air for this entire period was collected in one large bag, while in others the after-period

was subdivided into two periods of twelve and eight minutes respectively. In order to calculate oxygen debts accurately it was necessary to determine whether a twenty minute after-period was of sufficient duration to allow the subject to return to his original basal level. That this was the case is shown by table 1, from which it may be seen that the oxygen consumption had, after twelve minutes, always returned to within 10 per cent and usually within five per cent of the initial basal value.

Hill, Long and Lupton (1924) have shown that the carbon dioxide excretion may not become stabilized for many minutes after exercise and we have not used the long after-periods which are necessary for a complete picture in this respect. Therefore, the figures for excess carbon dioxide represent only rough approximations and not actual values.

At the time of each observation the subject was classified according to the amount of edema present and also according to the apparent distress during the

TABLE 1

The oxygen consumption before and (twelve to twenty minutes) after stair climbing

Subject	Date	Before	After*	
		cc. per minute	*cc. per minute*	
C. P.	January 7, 1929	237	232	Normal subjects
T. H.	November 30, 1928	213	230	
E. J.	December 2, 1928	183	198	
C. T.	November 4, 1928	221	223	Subjects with severe congestive heart failure
J. R.	November 15, 1928	225	220	
F. H.	December 14, 1928	217	224	

* During the period from 12 minutes to 20 minutes after cessation of exercise.

exercise. In regard to edema one, two, and three plus marks have been used to denote: "pitting" of the ankles and feet only (+), "pitting" of the legs up to the knees (++), and "pitting" of the entire lower extremities (+++), respectively. "Dyspnea"—the term is used to mean subjective respiratory distress—has been classified according to our clinical impression of the amount of distress the patient suffered during and immediately after the exercise, supplemented by his own statement at the end of the experiment. Such a method cannot, of course, be quantitative, and it is quite possible to make an error between "+" and "++" but not between "+" and "+++."

The control observations were made on three healthy male subjects whose ages were 24, 25 and 29, respectively. All subjects had been fond of sports and athletics a few years previously but were out of training and in rather poor physical "trim" at the time the observations were made. In addition to stair climbing, two observations were made of the oxygen intake of normal subjects during and after standing-running.

Four of the patients who were studied suffered from hypertensive heart disease. Two of these had auricular fibrillation, a third had frequent ectopic beats without pulse deficit and the fourth regular rhythm. One subject had rheumatic heart disease with mitral stenosis. All the patients mentioned above were more or less "decompensated" when the experiments were performed and all of them had had one or more previous severe "breaks" in compensation. These individuals with chronic congestive failure were chosen because it is in such patients that one usually observes progressive inability to perform muscular work, and the object of this study has been to find the reason for this change. In addition, one cardiac patient who had never been "decompensated" was studied. This man had hypertension and syphilitic aortic insufficiency with moderate dyspnea on exertion. He also had diabetes mellitus. Observations were made on this patient during and after standing-running, as on the normal subjects.

RESULTS

Basal metabolic rates (table 2) were, with one exception normal or low. This finding in patients with congestive failure was rather surprising, for as has been mentioned, other observers have reported high values in such individuals. One of our patients (J. H.) had a high basal oxygen consumption, but he also had diabetes mellitus and had never had congestive failure. We are inclined to think that our patients had low basal metabolic rates because they were truly at their lowest metabolic level when the tests were made, and believe it possible that the high values which have been found by others may, in part at least, have been due to the lack of sufficient attention to those details which are necessary to insure complete physical rest and freedom from mental anxiety. One is more likely to obtain false high than false low values. The fact that the basal oxygen consumption of the normal subjects were also low seems to indicate that the conditions under which the observations were made were responsible for the low values obtained in the patients.

The basal oxygen consumption showed less variation in the patients than in the normal subjects. That basal metabolic rate may be unaffected by change in "compensation" is well illustrated by F. H. and J. R. (table 2), whose basal metabolic rates remained within the limits of error of the method used during various degrees of decompensation.

The clinical state during the exercise period was of considerable interest. Those subjects who had the most extensive edema (table 3,

C. T. and F. H.) had much more respiratory distress than did the individuals whose edema was limited to the ankles and feet. Both F. H. and C. T. were very coöperative individuals, and they gave every

TABLE 2

The basal metabolic rate

Subject	Date	Oxygen intake	Calories per hour per square meter	Basal metabolic rate	
		cc. per minute		*per cent*	
C. P.	November 12, 1928	233	37.0	−6	Normal subjects
	November 13, 1928	218	34.7	−12	
	November 29, 1928	237	37.0	−6	
	December 27, 1928	212	33.4	−15	
	January 6, 1929	230	37.5	−5	
	January 7, 1929	237	37.2	−6	
	January 10, 1929	221	35.2	−10	
	January 13, 1929	231	37.2	−6	
T. H.	October 21, 1928	254	41.2	+4	
	November 30, 1928	213	35.4	−10	
	January 14, 1929	273	42.1	+6	
E. J.	October 28, 1928	199	35.0	−11	
	December 4, 1928	183	32.4	−18	
J. S.	November 7, 1928	190	37.9	−4	
C. T.	December 4, 1928	221	36.8	−2	
R. P.	October 19, 1928	191	34.2	−7	
	October 22, 1928	178	32.7	−13	
		197	35.2	−6	
J. R.	October 23, 1928	214	37.8	+1	Patients with cardiac disease
	October 26, 1928	216	37.3	−1	
	November 15, 1928	225	38.5	+3	
	November 17, 1928	208	35.9	−4	
F. H.	December 14, 1928	217	34.2	−9	
	December 17, 1928	214	33.9	−10	
	December 18, 1928	203	32.2	−14	
	December 24, 1928	212	33.9	−10	
J. H.*	January 18, 1929	416	51.0	+32	
	January 19, 1929	357	43.7	+14	
	January 20, 1929	353	43.1	+12	

* J. H., the only subject whose basal metabolic rate was elevated, had diabetes mellitus. He was the only one of the patients who had never had congestive failure.

Basal metabolic rates were calculated according to Carpenter's tables. The rates were calculated on the basis of the weight when the subject had no visible edema.

indication of being completely "all in" at the end of the exercise. Despite his distress, C. T. was able to complete the exercise in the usual time but for F. H. this was impossible. This individual required six minutes and fifteen seconds to perform the same work which all other subjects did in two minutes and twenty seconds. After getting half way up the stairs he had to stop every few steps and pause for several seconds before he could proceed. His respiratory distress was at least equal to and probably greater than that of the normal controls in the much more severe exercise of standing-running. Psychic factors such as fear were certainly not the limiting factor in this man. His capacity to work was restricted by his respiratory distress. J. H., during standing-running, had considerable respiratory distress, but declared at the end that he "could have done more." Objectively, he appeared "all in."

The minute ventilation during the basal period varied in the normal subjects between 3.65 and 5.77 liters. The patients had greater ventilation—5.86 to 8.57 liters—and in general, the degree of difference was proportional to the severity of the patient's symptoms. J. H., the cardiac patient who had never been decompensated, had a basal minute ventilation of 6.92 liters.

The *excess ventilation* was calculated by subtracting the basal ventilation for the corresponding period from the total ventilation during the exercise plus that of the after-period (table 3). The excess ventilation for the stair-climbing exercise in the normal subjects was 18.4 to 43.6 liters. For the cardiac patients the values ranged between 41.1 and 113.7 liters. Those patients who had most edema (C. T. and F. H.) had the greater excess ventilation. The values for excess ventilation for standing-running for normal subjects were 220.4 liters and 299 liters, respectively, and for J. H., 278.2 liters. For stair-climbing, the excess ventilation per kilo was 0.32 to 0.68 liters in the normal subjects and 0.72 to 1.47 liters in the patients. For standing-running the excess ventilation of C. P. was 3.45 liters, that of T. H. was 4.68 liters and that of J. H., 3.09 liters per kilo. These findings are in agreement with those of other observers and indicate that the patient with congestive failure differs from the normal in the following respects: (a) his resting ventilation is greater; (b) his maximum ventilation is less; (c) for a given exercise he increases his ventilation

TABLE 3

The excess oxygen intake and the excess carbon dioxide excretion during and after exercise

Stair climbing. All subjects completed the exercise in 2.33 ± 0.1 minute

Subject	Date	Basal ventilation per minute	Excess ventilation during and after exercise	Excess ventilation per kilo	Excess oxygen intake			Oxygen requirement per kilo	Excess oxygen during exercise	Excess carbon dioxide excretion					CO_2 absorbed from 100 cc. of respired air			Edema	Dyspnea	Remarks
					During exercise	After exercise (debt)	Total (requirement)			During exercise	After exercise	Total excess CO_2	Total excess CO_2 per kgm.	Excess CO_2 during exercise	Basal period	During exercise	After exercise			
		liters	*liters*	*liters*	*cc.*	*cc.*	*cc.*	*cc.*	*per cent*	*cc.*	*cc.*	*cc.*	*cc.*	*per cent*	*cc.*	*cc.*	*cc.*			
C. P.	November 12, 1928	5.39	36.2	0.56	766	840	1,606	25	48						4.34	6.02	4.09	0	0	Normal
	November 13, 1928	4.80	29.4	0.46	1,034	1,000	2,034	32	51	500	680	1,180	18	42	4.55	6.42	4.76	0	0	
	November 29, 1928	5.58	23.6	0.37	813	792	1,605	25	51	600	910	1,510	23	39	4.25	6.01	4.50	0	0	
T. H.	October 21, 1928	5.12	42.9	0.67	1,171	780	1,951	30	60	750	760	1,510	24	50	4.96	5.34	4.73	0	0	Normal
	November 20, 1928	5.40	43.6	0.68	1,059	744	1,803	28	59	800	1,050	1,850	29	43	3.95	4.75	3.90	0	0	
E. J.	October 28, 1928	4.70	18.4	0.32	480	900	1,380	24	35						4.23	5.44	4.61	0	0	Normal
	December 2, 1928	3.65	35.2	0.62	836	792	1,628	29	51	550	820	1,370	24	40	5.00	5.54	4.85	0	0	
R. P.	October 19, 1928	6.68	61.6	1.07	876	1,720	2,596	45	34	510	1,390	1,900	33	27	2.86	3.26	3.27	+	+	Hypertension; auricular fibrillation
	October 22, 1928	5.96	41.1	0.72	690	775	1,465	26	47	630	760	1,390	24	45	2.56	2.78	2.80	+	+	
	October 24, 1928	5.86	64.6	1.14	624	700	1,324	23	47	580	2,400	2,980	52	19	3.36	3.03	2.90	+	++	
J. R.	October 23, 1928	7.66	72.4	1.25	607	800	1,407	25	43									+	+	Hypertension; ectopic beats
	October 26, 1928	7.30	56.6	0.98	675	980	1,655	29	41	460	790	1,250	22	37	2.96	2.98	2.94	+	+	
	November 15, 1928	8.57	53.2	0.94	859	456	1,315	23	65	750	990	1,740	31	43	2.63	2.76	2.65	+	++	
J. S.	November 7, 1928	7.22	66.9	1.47	366	1,140	1,506	33	24	340	1,270	1,610	35	21	2.63	2.72	2.49	+	++	Mitral stenosis regular
C. T.	December 4, 1928	8.24	81.8	1.37	440	962	1,402	24	31	830	1,530	2,360	40	35	2.68	1.84	2.51	++	+++	Hypertension regular
F. H.	December 12, 1928	6.13	113.7	1.41	1,143*	567	1,710	21	67*	1,770*	1,550	3,320	41	53*	3.53	2.57	2.78	+++	+++	Hypertension; auricular fibrillation. Required 6.25 minutes to complete stair-climbing exercise
C. P.	January 13, 1929	5.77	220.4	3.45	3,900	4,300	8,200	127	48	3,480	7,820	10,660	165	32	4.00	5.89	3.04	0	+++	Normal. Standing-running 250 "low" steps per minute for 2.33 minutes

T H.	January 13, 1929	4.70	299.0	4.68	5,790	6,840	12,630	198	46	4,110	5,110	9,220	144	45	5.82	4.61	4.50	0	+++	Normal. Standing-running 200 "high" steps per minute for 2.33 minutes
J H.	January 20, 1929	6.92	278.2	3.09	3,690	7,580	11,270	125	33	2,220	3,390	5,610	62	40				0	+++	Hypertension; cardiac enlargement. Standing-running 160 "low" steps per minute for 2.33 minutes

* The subject required 6.25 minutes to complete the stair-climbing exercise and the starred values are therefore not comparable to the findings in the other subjects, in all of which the duration of the exercise was 2.33 ± 0.1 minute.

more. J. H., who had never had congestive failure reacted as did the normal subjects, except for having a somewhat higher basal minute ventilation.

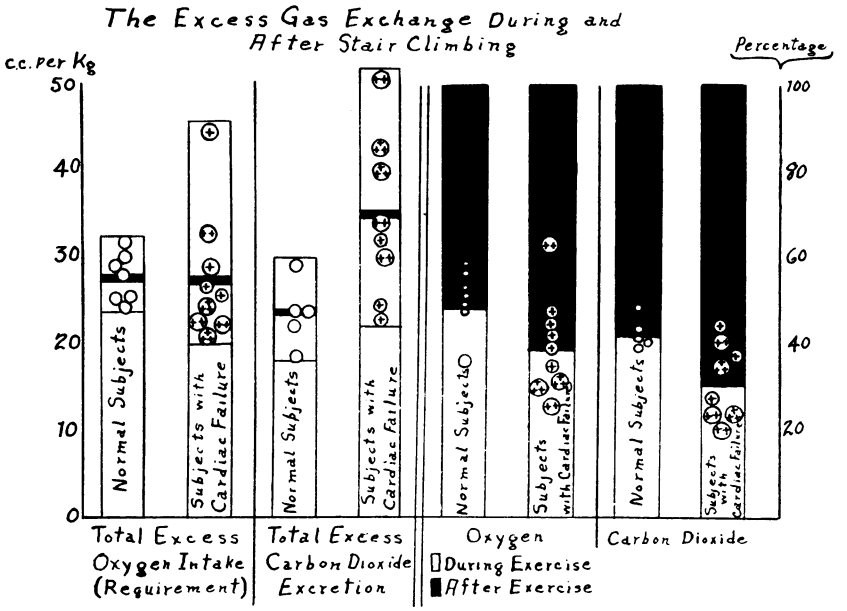

FIG. 1. The hollow circles indicate that the normal subjects experienced no distress during the exercise. The patients all had some distress, the degree of which is indicated for each experiment by the number of plus marks in the circle. The heavy cross bars show average values. The average oxygen requirement per unit of body weight is seen to be about the same in the control subjects and in the patients. One of the latter had a conspicuously higher value—error (?)—and several showed slightly lower figures than the controls. The average value was the same for the two groups.

The total excess carbon dioxide excretion is seen to be greater by almost 50 per cent in the patients than in the normal subjects. Those patients who had the most discomfort had ordinarily the highest values for carbon dioxide excretion.

In the right half of the chart the distribution of the excess gas exchange is indicated. The black areas represent average excess gas exchange after exercise, and the unshaded areas denote average values during exercise. The patients had relatively less oxygen intake and carbon dioxide excretion during the exercise and consequently their excess gas exchange after the exercise was greater. The limitation of oxygen intake during exercise is correlated with the degree of distress, but no such correlation is seen in the case of carbon dioxide.

The excess oxygen intake during the stair-climbing exercise varied between 480 cc. and 1171 cc. in the normal subjects. In the cardiac patients the values were from 366 cc. (J. S.—mitral stenosis) to 876 cc. The excess oxygen intake during standing-running was 3900 cc. and 5790 cc. for normal subjects, C. P. and T. H., respectively, and 3690 for J. H.

The oxygen debt in the patients was 456 to 1720 cc. for the milder exercise (stair-climbing). The normal subjects had debts of 744 to 1000 cc. After standing-running the oxygen debts of the normal individuals were 4300 cc. and 6840 cc., (table 3) respectively, and of J. H., 7580 cc.

The oxygen requirement for the stair-climbing exercise was 1315 to 2596 cc. for the patients. The highest values for debt and requirement were obtained in the same patient (R. P.) and only on one occasion. The other values for debt and requirement were considerably lower and all fell nearly within the normal limits. For the same exercise the normal subjects used 1380 to 2034 cc. of excess oxygen, but their oxygen requirements for standing-running were 8200 and 12,630 cc., respectively, and that of J. H. was 11,270 cc. When expressed in terms of cubic centimeters per kilogram of body weight the oxygen requirement for stair-climbing was 24 to 32 for the normal subjects and 21 to 45 for the patients, the latter value being the only one conspicuously outside the range of the normal subjects. The average values for the patients and the controls were the same: 27 cc. per kilogram. The oxygen requirements for standing-running were 127 and 198 cc. per kilo for the normal subjects and 125 cc. for J. H. The percentage of the oxygen requirement which was consumed during the exercise was very variable both in the normals (35 to 60 per cent) and in the patients (24 to 65 per cent). In general, the normal subjects took in about 50 per cent of the oxygen required during the exercise (and this held true even for the severe exercise of standing-running), whereas, in the patients, oxygen debt although variable was a somewhat higher and the exercise intake a somewhat lower percentage of the total requirement than in normal subjects. J. H., in this respect, fell in with the "decompensated" patients: for the standing-running exercise, he took in only 33 per cent of his total requirement during the exercise.

With regard to oxygen intake the findings may be summarized as follows:

1. For a given exercise performed in a given time the individual with congestive heart failure is abnormal in the following respects (fig. 1):

a. His oxygen intake during the exercise is somewhat diminished (this phenomenon was apparently more marked in a patient with mitral stenosis than in those with hypertension).

b. His oxygen debt is usually a disproportionately large fraction of his total requirement.

c. His oxygen requirement may be elevated but is usually within normal limits.

2. For exercise of nearly maximal severity (C. T. and F. H. stair-climbing as compared to C. P. and T. H. standing-running (fig. 2): (a) his oxygen intake during the exercise; (b) his oxygen debt, and (c) his oxygen requirement, are very much reduced.

The excess carbon dioxide excretion during exercise varied between 500 and 800 cc. in the normals. The values in the cardiac patients fell in, or nearly in, this range with one exception, when the exercise time was kept constant. J. S. (mitral stenosis) had a distinctly lower value (340 cc.). Except for J. S., who had fairly severe respiratory distress, the excess carbon dioxide excreted during the exercise was proportional to the degree of discomfort experienced. This suggests that the physiological basis for the distress may have been different in J. S. from that in the other subjects and this point will be discussed later. During the standing-running, the normal subjects excreted 400 to 500 per cent (and J. H. almost as much) more carbon dioxide than did the cardiac patients during stair-climbing.

The excess carbon dioxide excretion after exercise was usually considerably greater in the patients than in the normal subjects for stair-climbing, but was very much less than that of the normals after standing-running (table 3).

The *total excess carbon dioxide excretion* was greater in the patients (1250 to 3320 cc.) than in the normals (1180 to 1850 cc.). Per kilogram of body weight the values were 18 to 29 cc. for the normals and 22 to 52 cc. for the patients. In figure 1 the average values are seen to be 24 cc. in the normals and 35 cc. in the patients and it is clearly shown that the amount of carbon dioxide excreted was pro-

portional to the degree of distress, whereas, the oxygen requirement was not. The maximal carbon dioxide excretion of the normal subjects and of J. H., who were able to perform much more strenuous

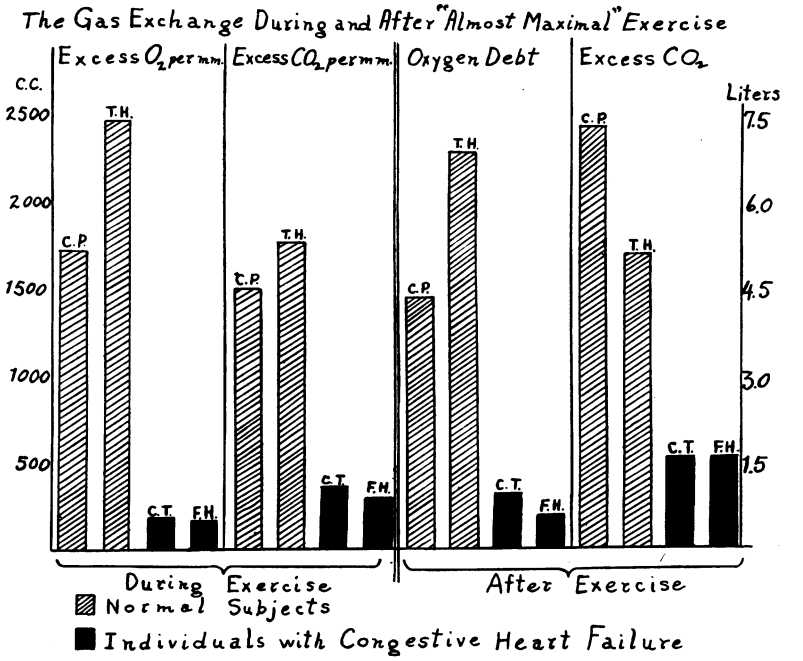

FIG. 2. All subjects had severe distress but C. P. and T. H. did much more strenuous work (standing-running at a rapid rate as compared with slowly ascending and descending one flight of stairs). The maximum oxygen intake of the normal subjects was much greater than that of the patients. However, the maximum oxygen debts were also low in the patients and this fact indicates that diminished oxygen intake during the exercise could not have been the essential limiting factor. The actual carbon dioxide excretion was much less in the patients than in the control subjects but the "non oxidative" carbon dioxide was relatively much greater.

work, was much greater than that of the patients when doing their maximum work. (Table 3 and fig. 2.)

The percentage of the total excess carbon dioxide which was excreted during exercise was 39 to 50 in the normal subjects and 19 to 45 in the

patients. The average values were 43 and 32 per cent, respectively, leaving a larger proportion to be excreted after cessation of exercise in the patients than in the normals.

Individuals with congestive cardiac failure may, therefore, behave abnormally in regard to carbon dioxide in the following ways:

1. For a given exercise:

a. The total excess carbon dioxide excreted is usually greater.

b. Although, in general, the increase in carbon dioxide excretion parallels the degree of distress, this is not necessarily true as a subject may have considerable discomfort and excrete, during the exercise, considerably less than the normal amount.

c. The proportion excreted during exercise is diminished.

2. *For exercise of nearly maximal severity*, the carbon dioxide excretion is much less than in the normal subjects.

With respect to carbon dioxide, the findings in J. H., who had never been decompensated, were similar to those of the normal subjects throughout.

The oxygen absorbed per unit of ventilation was diminished in the patients both during rest and during exercise (table 3). The normal subjects, in addition to starting with a greater oxygen absorption for a given ventilation than the patients, increased their efficiency of breathing during exercise. The single exception to this was found in T. H. during standing-running in which he "broke" in this respect and absorbed a smaller proportion of the inspired oxygen than at rest. In this respect, T. H., during severe exercise, was similar to the cardiac patients. The latter, starting with a lower "respiratory utilization," were unable to increase their efficiency and the cases which had most distress (C. T. and F. H.) became even less efficient, exhibiting a rise in the oxygen content of their expired air. J. H. was even more efficient than the normal subjects.

DISCUSSION

No attempt will be made at this time to interpret the significance of the changes in ventilation.

It has been shown that our patients with congestive failure usually had a normal basal metabolic rate and that under conditions of exercise the oxygen requirement may be elevated but usually was with-

in the limits observed for normal subjects for the same exercise. Other observers have found high basal oxygen consumption and increased oxygen requirement in patients with congestive failure, but the fact that such phenomena were not the rule in our patients suggests the possibility that even when they are present they are due to other factors and are not an essential event in the progress of heart failure. Our findings support the suggestion of Herbst and are contrary to the views of Eppinger and his coworkers, who regard disturbed resynthesis of glycogen from lactic acid and, hence, increased oxygen consumption as one of the most important factors of heart failure.

The distribution of the oxygen in relation to phases of the observations was somewhat altered. On the whole, our cardiac patients absorbed a smaller proportion of their total excess oxygen during the exercise and their debts were correspondingly greater, averaging 60 per cent as compared to 50 per cent in the normal subjects. This finding suggests that our patients were relatively unable to increase their minute cardiac output. This may have been due to the fact that they were all receiving digitalis: the drug rather than the disease may have been the responsible factor. Digitalis decreases the cardiac output of normal dogs (Harrison and Leonard, 1926; Cohn and Stewart, 1928), and of normal men (Burwell, Neighbors and Regen, 1927). Its effect in patients with congestive failure must still be regarded as an open question but we believe that the available evidence indicates a similar action (Eppinger, von Papp and Schwarz, 1924; Harrison and Pilcher, 1930). If digitalis does have such an action it may also tend to prevent increase in output. There is no good evidence for or against such a view and it is simply suggested as one possible causative factor.

Another possible factor in the causation of the high debt fraction found in some of our patients must be considered. In the first paper of this series (Harrison and Pilcher, 1930), it was shown that oxygen utilization may be diminished in edematous tissues. In this case it is obvious that the increase in oxygen requirement necessitated by exercise will demand a disproportionately large increase in the volume flow of blood through the edematous tissues and hence probably also a correspondingly increased minute cardiac output. Should the heart be unable to increase its output to so great an extent, for the reason

suggested above or for any other (see below), the excess oxygen intake during exercise must be diminished and the oxygen debt proportionately increased. On the other hand, even if the heart were capable of such an increase in output, the diminished utilization caused by edema must result in a corresponding limitation of oxygen intake during exercise.

If this be true, that is, if edema itself be an important cause of the relatively higher oxygen debts found in our patients, one would expect the oxygen debts to vary directly and the excess oxygen intake during exercise inversely with the degree of edema present. The data in table

TABLE 4

The excess gas exchange per minute during exercise

Subject	Date	Edema	Dyspnea	Excess oxygen intake during exercise	Excess carbon dioxide during exercise	
				cc. per minute	*cc. per minute*	
C. P.	November 29	0	0	349	257	Normal subjects
T. H.	November 30	0	0	454	343	
E. J.	December 2	0	0	358	236	
R. P.	October 19	+	+	376	219	Patients with congestive failure
	October 22	+	+	296	270	
	October 24	+	++	263	249	
J. R.	October 28	+	++	289	197	
	November 15	+	++	369	322	
J. S.	November 7	±	++	157	146	
C. T.	December 4	++	+++	189	356	
F. H.	December 14	+++	+++	183	288	

4 show this to be true with one exception. The excess oxygen intake during exercise of C. T. and F. H., who had more edema than the other patients studied, was much lower than any other except J. S., and that of the other patients was almost invariably lower than that of the normal subjects. In the case of J. S., who had little or no edema, another factor is present: he was the only patient studied who had mitral stenosis, and his lesion was presumably of high degree, since his murmur lasted throughout diastole. It seems likely that the inability to increase the output of his heart which he presumably had was on the basis of this lesion, rather than of edema. The findings in him are in

accord with those of Meakins and Long (1927) in similar cases and offer support for the point of view which Burwell (1929) has expressed, namely that different subjects with heart disease have different types of functional disability and that the distress on exertion of "compensated" individuals with mitral stenosis may be primarily due to an incapacity, because of mechanical obstruction, to increase sufficiently the output of the heart.

Our findings on J. H. indicate that the diminution in cardiac reserve may be present in "compensated" as well as in "decompensated" cardiac patients. This man, who had never had peripheral or pulmonary congestion and who was able to perform exercise comparable to the maximal exercise of the normal subjects, nevertheless took in only 33 per cent of the total oxygen requirement during the exercise, as compared with 46 and 48 per cent, respectively, for the normal individuals. These findings are in accord with the conclusions of Meakins and Long and of Herbst regarding "compensated" patients.

Although the total oxygen requirement was usually normal in our patients, the total excess carbon dioxide was distinctly increased, by about fifty per cent as an average. We are inclined to attach considerable importance to this finding.

As has already been stated, it has not been possible for us to follow our patients for the long after-periods which, as Hill and his co-workers have shown (1924), elapse before the carbon dioxide excretion returns to its original level. During and immediately after severe exercise the carbon dioxide excretion rises to a greater degree than does oxygen intake, because, in addition to that increase which is an expression of greater oxidation, some carbon dioxide is freed from carbonate and excreted in the process of buffering lactic acid. With exercise of increasing severity this "displaced" carbon dioxide becomes an increasingly large fraction of the total excreted. During the latter stages of the recovery period the lactic acid which had displaced carbon dioxide is burned, less carbon dioxide is excreted than is produced and carbonates are reformed as lactates disappear. Consequently, the extent of elevation of the carbon dioxide excretion, as compared to the oxygen intake is a measure of the degree of carbonate depletion and hence of the degree of "acidosis" during exercise, and the later depression of carbon dioxide excretion affords a similar measure of carbonate

replacement. The sum of the two should be zero. Because of the relatively short durations of our after-periods, (which were long enough to obtain the complete "picture" for oxygen but not for carbon dioxide), the final phase was not obtained and hence what we have called "total excess carbon dioxide" merely means the excess during the time of observation.

Despite this limitation the data are fairly conclusive. In figure 3, it is seen that the excess carbon dioxide excretion is much greater in the patients than in the normal subjects but that the elevation comes in the exercise period and in the first after-period, and that in the second after-period their excretion is practically the same as that of the normal subjects. Since the total oxidation is not usually altered, it does not seem possible to explain this phenomenon in any way other than by assuming that more preformed carbonate is used to buffer lactic acid in the patient with congestive failure than in the normal subject. The other possibility—that more lactic acid is produced—is rendered unlikely by our values for oxygen consumption. It is difficult to see how such an event could take place unless the non-carbonate buffers of the tissues were diminished in amount.

Such an interpretation is in accord with the conclusions of Eppinger, Kisch, and Schwarz, who first suggested that the cardiac patient suffered from diminished tissue buffering power, their evidence being that the lactic acid content, the C_H, and the oxygen dissociation curves of the blood were all more affected by exercise in their patients than in normal subjects. However, these authors were inclined to regard carbonate depletion and consequent hypocapnia as an important factor, while our data seem to indicate that it is the non-carbonate buffers which are affected. Furthermore, Eppinger and his co-workers found greater oxygen requirements for their patients, and concluded that the ability of the tissues to resynthesize glycogen from lactic acid was impaired. They attributed great importance to this phenomenon, which our patients as a rule did not exhibit.

The "distribution" of the excess carbon dioxide is of interest (fig. 1). The normal subjects excreted as an average 43 per cent of their total excess carbon dioxide during the exercise, and this was a distinctly larger proportion than was observed in the patients, in whom the range was lower and the average value was 32 per cent. However, the actual

amounts excreted per minute during exercise were about the same in the patients as in the control subjects. The only conspicuous excep-

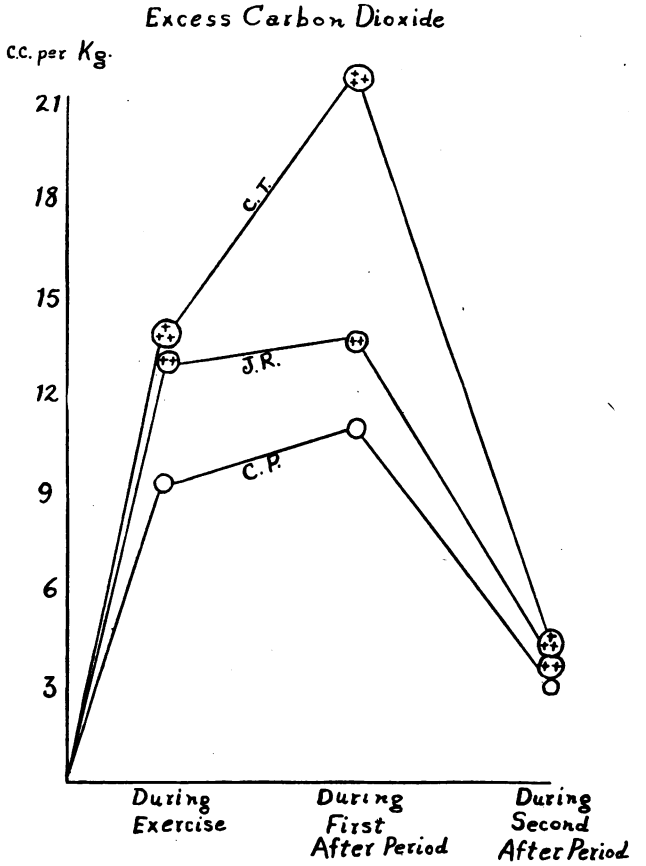

FIG. 3. Time relationships are neglected. Patients with moderate (J. R.), or severe (C. T.) distress are compared with a normal subject (C. P.), who experienced no discomfort. The exercise was in each case the same (stair-climbing). The patients are seen to have a greater carbon dioxide excretion but the increase comes during the exercise and in the first after-period. During the second after-period all subjects have comparable values. The fact that the greater rise in carbon dioxide excretion comes during and soon after exercise is compatible with the view that it is due to a "blowing off" from acidosis and this in turn is believed to be due to a diminution in the non-carbonate buffer.

tion in this regard was J. S. (table 4), who had a much lower rate of carbon dioxide excretion during exercise than any other subject studied. As was pointed out in the discussion of oxygen intake, there is good reason to believe that this man, who had mitral stenosis, was suffering primarily from inability to increase his cardiac output. His very low carbon dioxide excretion during exercise, whether considered relatively or as an absolute value, seems to support this view. This man had severe distress, about equal to that of J. R. at the last time he was studied, but not as great as that of C. T. and F. H. However, the latter three subjects, despite their great distress, excreted more carbon dioxide during the exercise than any of the other subjects and their values for oxygen intake per minute were greater than that of J. S. F. H. and C. T., the subjects with the greatest distress and the most edema, took in oxygen at a rather slow rate during the exercise, but, as has already been explained, this may have been due to the edema *per se*. J. R., on November 15th, had slight edema and moderate distress, about equal to that of J. S., but J. R., during the exercise, absorbed oxygen and eliminated carbon dioxide at about twice the rate of J. S. Furthermore, J. R., whose clinical state as regards dyspnea was distinctly worse on November 15th than on October 28th (table 4), had a greater gaseous exchange when he was in poorer clinical condition. We do not see how these findings can be interpreted other than by assuming that J. S. had a different cause (limitation of output) for his distress than did F. H. and C. T. (limitation of utilization and acidosis) and J. R. (acidosis).

Thus far, the patients with congestive heart failure have been contrasted with normal subjects performing the same exercise. When a comparison is made between those patients who were at or near their maximum level of work with normal subjects who were approaching their highest level of exercise, other interesting points are noted. It is important in this connection that the distress suffered by the normal subjects and the "compensated" patient J. H., during standing-running is definitely comparable to that suffered by the patients C. T. and F. H., who had the most marked edema, during the stair-climbing exercise. If the distress of one group predominated at all over that of another, it was greater in C. T. and F. H. The normal individuals and J. H. were extremely dyspneic and fatigued; C. T. and F. H. were "all in."

As is seen in the left half of figure 2 the normal subjects were able to take in about ten times as much oxygen and to excrete about five times

TABLE 5

The oxygen consumption before and after "maximal" exercise

Subject	Date	Type of exercise	Oxygen intake				
			Before exercise	During exercise	During the first after period	During the second "after" period	
			cc. per minute	*cc. per minute*	*cc. per minute*	*cc. per minute*	
C. P.	January 13, 1929	Standing-running 250 "low" steps per minute for 2.33 minutes	231	1,964	537	283	Normal subjects
T. H.	January 14, 1929	Standing-running 200 "high" steps per minute for 2.33 minutes	273	2,760	780	368	
C. T.	December 4, 1928	"Routine" stair climbing exercise in 2.33 minutes	221	383	300	233	Subjects with severe congestive heart failure
F. H.	December 14, 1928	"Routine" stair climbing exercise in 2.33 minutes	217	400	263	244	
J. H.	January 20, 1929	Standing-running 160 "low" steps per minute for 2.33 minutes	353	1,935	718	495	Hypertension; cardiac enlargement; diabetes

* The first "after" period lasted for twelve minutes immediately after the exercise. The second "after" period embraced the succeeding eight minutes.

as much carbon dioxide per minute as were the patients when suffering at least as much physical distress. This difference may have been due in part to inability to increase the cardiac output and one might be

disposed to consider this as the sole factor. However, emphasis has already been laid on the fact that the oxygen intake is limited not only by circulation but by utilization, and as both patients had edema of considerable degree it is entirely possible that decreased utilization, due to edema, may have been an additional factor. Diminution in oxygen supply during exercise can only cause distress, however, by diminishing oxidation causing lactic acid accumulation and if the distress of the patients had been due to decreased oxidation, whether from impairment of cardiac output or utilization or both, one would expect that their oxygen debts would be equal or nearly equal to those of normal subjects. But this was not the case, as is shown in the right half of figure 2. The oxygen debts were seven or eight times as great in the normal subject as in the patients and the latter only excreted about one fourth as much excess carbon dioxide after the exercise. It is therefore obvious, since the patients had much smaller oxygen debts, that diminished oxygen intake during exercise could not have been the chief limiting factor in the patients. The data indicate clearly that *the limiting factor was inability to accumulate an oxygen debt.*

The next question which arises is: What determines the ability to accumulate an oxygen debt? The answer is to be found in the studies of Hill and his co-workers. Hill and Lupton (1923) stated: "Apparently the limit is set by the rise in the hydrogen ion concentration (C_H) affected by the presence of the lactic acid itself, and may be increased if the rise of C_H be hindered by the presence of extra alkali." They also said: "There remains, however, one simple chemical factor, the efficiency of buffering of the muscles, which determines the fatigue maximum of lactic acid, the maximum oxygen debt, and therewith the extent and duration of a short-lived violent effort." Our subjects could scarcely be said to have been making "violent" effort but they were all performing exercise near their maximal level and none of them were in a "steady state." Under such conditions their oxygen debts must have been close to their greatest possible values. The values for total oxygen consumption show that much more lactic acid was produced in the normal individuals during standing-running, and as the distress of all subjects seemed to be roughly the same, it is probable that far less lactic acid was buffered by the muscles of the patients than by those of the normal subjects.

It is of great interest that the patient J. H., who had never had congestive failure, was able to accumulate an oxygen debt of 7580 cc., which is greater than that of the normal subjects studied after maximal exercise. The fact that this was possible in spite of the limitation of output which we believe he had, as previously discussed, and that he had never had edema, suggest that edema *per se* may be a cause of the limitation of ability to accumulate an oxygen debt. Further data bearing on this subject will be presented in the following papers of this series.

As was stated in the first paper of this series, we have undertaken to study heart failure by an analysis of the underlying causes of the patients' symptoms. In the present publication, diminished tissue buffering power has been suggested as a possible element in the causation of dyspnea on exertion. It should be clearly stated here that we do not believe diminished buffering power to be the essential cause of congestive heart failure—or at least not the cause of the first "break." We believe a diminished buffering power to be originally an effect of congestive failure but quite possibly an important cause of further "breaks."

SUMMARY AND CONCLUSION

Under basal conditions the individuals with congestive cardiac failure whom we have studied had increased ventilation but their metabolic rates were usually normal. Exercise which produced no discomfort in normal subjects caused distress in the patients and the degree of distress was usually proportional to the amount of edema. The ventilation increased more in the patients. The oxygen intake during the exercise was usually somewhat less and the oxygen debt correspondingly greater than in normal subjects. The total oxygen requirement was usually not changed. The excess carbon dioxide production during the exercise was often slightly greater and immediately after the exercise it was usually considerably greater than in normal subjects. The patients with the most edema had the greatest carbon dioxide excretions.

The maximal exercise of which "decompensated" patients were capable was much less than for normal men. Maximal values for oxygen intake during exercise and for oxygen debt were much less in

the patients than in the normal subjects. Maximum ventilation was also less.

One cardiac patient who had never been "decompensated," on performing maximal exercise, had an oxygen requirement and oxygen debt comparable to those of normal individuals but had a ratio of oxygen intake during exercise to oxygen debt comparable to that of the decompensated patients.

One patient with mitral stenosis and only slight edema had a lower oxygen intake and carbon dioxide excretion during exercise than any other subject studied.

From these findings the following conclusions are drawn:

1. Subjects with mitral stenosis and only slight edema may suffer primarily from inability to increase their cardiac outputs per minute.

2. Subjects with edema and hypertensive heart disease may suffer from (*a*) a low maximum cardiac output; (*b*) impairment of oxygen utilization, so that with a given cardiac output per minute the oxygen intake is less; (*c*) diminished buffering power of the tissues.

3. In patients who have had edema of severe degree for a long time, the limiting factor, in so far as gas exchange is concerned, does not appear to be decreased oxygen intake but inability to acquire a large (normal) oxygen debt, and this discrepancy is believed to be due to impairment of tissue buffering power.

We would like to emphasize our indebtedness to Professor Hans Eppinger and his co-workers, Dr. Daniel Laszlo and Dr. Heinrich Schwarz. Although our findings differ from theirs in certain respects, our interpretations as regards tissue buffering power agree with their conclusions.

It is a pleasure to thank Dr. Glenn E. Cullen for valuable suggestions and kindly criticism.

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