THE EFFECT OF THE DIGITALIS BODIES ON THE VELOCITY OF BLOOD FLOW THROUGH THE LUNGS AND ON OTHER ASPECTS OF THE CIRCULATION. A STUDY OF NORMAL SUBJECTS AND PATIENTS WITH CARDIOVASCULAR DISEASE[1]

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Knowledge of the efficiency of the circulation in man before and after the administration of therapeutic measures is essential to establish a rational basis for the treatment of circulatory failure. Circulatory measurements in normal subjects and in patients before and after the administration of digitalis bodies are few. Burwell, Neighbors, and Regen (1) studied the changes in the minute volume output of the heart after the administration of large therapeutic doses of digitalis powder to four normal subjects. Following the administration of digitalis they observed, by the method of Field, Bock, Gildea, and Lathrop (2), no increase in the cardiac output per minute. On the contrary there was a slight but definite reduction of blood flow. The decrease in blood flow, according to these authors, could not be explained by the normal variation in the volume of blood expelled from the left ventricle per minute, or by technical error. In applying their results to patients with circulatory failure, they caution, however, that "If the same pharmacological effect upon heart muscle can produce different effects upon cardiac output in different states of heart muscle, it is then unsafe to apply our conclusions directly to an analysis of the effect of digitalis upon the cardiac output of patients suffering from heart failure." Eppinger, Papp, and Schwarz (3) observed a reduction in the amount of blood expelled from the left

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ventricle of one patient who was suffering from circulatory failure. No significance can be attached to this finding for it is well recognized that the method they used does not give reliable results in patients with circulatory failure. Cohn and Stewart (4) studied the effect of digitalis by means of moving x-ray films, observing the change in the height of the left ventricular excursion of the heart. The four patients studied were young adults with symptoms and signs of rather mild circulatory failure. Two of the patients showed auricular fibrillation, the other two regular rhythm. In all four patients a significant increase in the height of the left ventricular excursion was seen, when the patients were under the effect of digitalis. An increase in the ventricular excursion, under such conditions, does not necessarily indicate, but is suggestive of increased output of the heart, provided that there is no corresponding decrease in rate, and provided there is no significant change in the size of the heart. Recently Hochrein and Meier (5), applying Bromser's method on man, noted that, following the administration of strophanthin, patients suffering from circulatory failure showed a decrease between the peaks of the pulse and pulse velocity curves simultaneously taken. This indicates that, following the administration of therapeutic doses of strophanthin, the blood flow through the radial arteries increased. Kininmonth (6) using Henderson's ethyl iodid method observed that the circulation rate may be increased, decreased, or unaffected by digitalis in patients with diseased circulatory system. These variations in reponse to giving digitalis occurred not only in different patients, but in the same patient at different times. An increase in the circulation rate was more apt to occur in patients with low circulatory rate and with signs of circulatory failure. In patients with heart disease, but with no reduction of the circulatory rate, an increase occurred less frequently and the circulation rate was either unaltered or decreased. It should be recalled that the value of the ethyl iodid method in the form applied by Kininmonth has been adversely criticised.

In view of these discrepant results, and the questionable reliability of the methods applied by some of the investigators, one is forced to conclude that the effect of digitalis on the blood flow in man and in patients with circulatory failure remains unknown.

Because preceding studies (7) have shown that the velocity of blood flow is a fundamental and characteristic aspect of the circulation both in health and in disease, and because a reliable method for the measurement of the velocity of blood flow has become available, we have investigated the effect of digitalis on the velocity of blood flow in normal subjects as well as in patients with cardiovascular disease.

METHODS

The methods employed in this investigation were similar to those used in previous studies (8). Simultaneously with the measurement of the velocity of the blood flow through the lungs, the velocity of venous blood flow from the right elbow to the right auricle was measured. The venous pressure was estimated by the method of Moritz and Tabora (9), and the vital capacity of the lungs with a Collins spirometer. All measurements were performed after more than 12 hours of eating the last meal.

RESULTS

A. In normal subjects

To ascertain the effect of the digitalis bodies on the velocity of blood flow of normal human beings, eight volunteer male subjects between the ages of 24 and 46 were studied (table 1). To observe the immediate effect of the administration of digitalis bodies, four of the subjects received strophanthin intravenously. The physiological activity of the specimen used was 0.14 mgm. per cat unit, as estimated by the assay of Hatcher and Brody (10). The velocity of the blood flow and other aspects of the circulation were measured before and again after the administration of the strophanthin. In subjects 4, 6, and 8 the measurement of velocity was repeated three hours after injection of the drug, while in subjects 3 and 5 the tests were repeated six hours after the administration of strophanthin. Subjects 1, 6, and 7 received large therapeutic doses of tincture of digitalis by mouth. The physiological potency of the tincture used corresponded to 1 cat unit per 1 cc. Subjects 1 and 6 received an initial dose of 50 per cent of the total dose at once, followed by two doses

TABLE 1

Effect of digitalis on the velocity of pulmonary blood flow of normal subjects

Number	Name	Age		Date	Heart rate per minute	Arm to heart circulation time		Pulmonary circulation time		Medication	Method of administration
						Seconds	Change, seconds	Seconds	Change, seconds		
				1927							
1	V. F.	46	Before	March 16	70	6.5	+3.5	14.0	+3.5	Tr. dig. 19 cc.	Mouth
			After	March 17	58	10.0		17.5			
2	W. H.	35	Before	January 19	103	5.5	+0.5	8.0	+0.5	Stroph. 0.9 mgm.	Vein
			After	January 19	91	6.0		8.5			
3	J. M.	35	Before	January 18	83	5.0	+0.5	8.0	0.0	Stroph. 0.7 mgm.	Vein
			After	January 18	93	5.5		8.0			
4	J. D.	24	Before	January 18	79	7.5	+4.5	11.5	0.0	Stroph. 0.9 mgm.	Vein
			After	January 19	83	12.0		11.5			
5	C. W.	35	Before	January 19	112	6.0	+2.0	8.5	−0.5	Stroph. 0.7 mgm.	Vein
			After	January 19	97	8.0		8.0			
6	F. D.	41	Before	January 16	55	13.0	+4.5	12.0	−1.0	Tr. dig. 17 cc.	Mouth
			After	January 17	57	8.5		11.0			
7	E. F.	24	Before	January 6	59	5.0	+0.5	8.5	−2.5	Tr. dig. 20 cc.	Mouth
			After	January 18	54	5.5		11.0			
8	M. M.	35	Before	January 19	111	5.0	−1.0	10.0	−2.5	Stroph. 0.9 mgm.	Vein
			After	January 19	100	4.0		7.5			

of 25 per cent of the total calculated dose at six hour intervals. The circulatory tests were performed six hours after the last dose. Subject 7 received tincture of digitalis in the same manner as just described. Circulatory measurements in the case of this individual were performed 12 hours after the administration of the last dose, when this normal person showed electrocardiographic evidence of the effect of digitalis. The same measurements were repeated twelve days later, when the dose of digitalis previously administered had probably been eliminated. Toxic reactions except for nausea and vomiting in subjects 1 and 7 were not observed. Table 1 illustrates that although there was a variation in dosage and method of administration of the digitalis bodies, the velocity of the blood flow showed no significant alteration. The average difference between the circulation time of the venous blood flow from the cubital vein to the right side of the heart was an increase of 1.9 seconds; the average difference between the pulmonary circulation times of the eight normal subjects studied was a decrease of 0.3 second. The maximum variation before and after the administration of the digitalis bodies was an increase of 4.5 seconds in the venous circulation time, and an increase of 3.5 seconds in the pulmonary circulation time. We have called attention to the fact that the velocity of the venous blood flow from the arm to the right side of the heart shows greater spontaneous variations both in normal individuals and in patients with circulatory failure, than the velocity of the blood flow in the pulmonary circuit (8). The arterial and venous blood pressures, as well as the vital capacities of the lungs of the eight subjects studied, showed no changes which could be attributed to a digitalis effect.

B. In patients with cardiovascular disease

The results of the investigation of the effect of the digitalis bodies on the velocity of blood flow of patients suffering from cardiovascular disease is presented in table 2. A summary of the clinical observations concerning the cardiovascular system of the 14 patients is appended at the end of this publication. It is evident that both the abnormality of the cardiovascular system and the degree of circulatory failure varied considerably. Patients 7, 8, 9, 10, 11 and 14 exhibited only symptoms and signs of circulatory failure on exertion,

TABLE 2

Effect of digitalis bodies on the velocity of pulmonary of blood flow of patients suffering from cardiovascular diseases

Number	Name	Age	Diagnosis		Date	Pulse	Venous pressure	Vital capacity per square meter	Arm to heart circulation time		Pulmonary circulation time		Medication	Method of administration
									Seconds	Change, seconds	Seconds	Change, seconds		
							cm. H_2O	*cc.*						
1	J. M.	62	Myocardial degeneration	Before	March 6	100	+9.0	800	22.0	−6.0	45.0	−13.0	Tr. dig. 16 cc.	Mouth
				After	March 8	72	+6.5	900	16.0		32.0			
2	J. C.	57	Myocardial degeneration	Before	February 23	84	+5.5	1,361	13.0	0.0	16.5	−8.0	Tr. dig. 22 cc.	Mouth
				After	February 23	87	+4.0	1,951	13.0		8.5			
3	P. F.	63	Arterial hypertension; myocardial degeneration	Before	May 12	81	+4.5	1,790	8.0	0.0	21.0	−7.0	Tr. dig. 16 cc.	Mouth
				After	May 14	73	+2.0	1,790	8.0		14.0			
4	C. B.	41	Arterial hypertension; myocardial degeneration	Before	May 18	118	+21.0	650	22.0	−15.5	22.0	−6.0	Tr. dig. 20 cc.	Mouth
				After	May 21	82	+6.5		6.5		16.0			
5	T. J.	52	Generalized arteriosclerosis; myocardial degeneration	Before	February 15	74	+4.5	1,960	10.0	+2.0	22.0	−5.0	Tr. dig. 18 cc.	Mouth
				After	February 17	68	+2.0	1,960	12.0		17.0			
6	P. M.	50	Myocardial degeneration	Before	May 12	64	+3.5	964	11.0	+4.0	14.5	−4.5	Tr. dig. 21 cc.	Mouth
				After	May 16	58	−1.0	1,384	15.0		10.0			
7	A. S.	74	Arterial hypertension; myocardial degeneration	Before	March 6	78	+5.5	2,330	9.0	+5.0	24.5	−4.5	Tr. dig. 16 cc.	Mouth
				After	March 8	66	+2.0	2,610	14.0		20.0			

8	P. P.	68	Auricular fibrillation; arterio-sclerosis	Before After	February 13 February 15	88 75	+5.5 +5.5	2,230 2,230	10.0 8.0	−2.0	15.5 12.0	−3.5	Stroph. 1.0 mgm.	Vein
9	W. M.	65	Syphilitic heart disease; aortic insufficiency	Before After	March 8 March 10	72 74	+2.0 +2.5	2,000 1,950	10.0 7.0	−3.0	17.0 16.0	−1.0	Tr. dig. 19 cc.	Mouth
10	A. O.	68	Arterial hypertension; myo-cardial degeneration	Before After	January 6 January 6	78 60	+7.0 +10.5	1,790 1,440	10.0 8.5	−1.5	13.0 15.0	+2.0	Stroph. 0.8 mgm.	Vein
11	W. P.	39	Syphilitic heart disease; aortic insufficiency	Before After	March 8 March 10	84 72	+1.0 +1.0	2,130 2,090	5.0 5.5	+0.5	12.0 14.0	+2.0	Tr. dig. 17 cc.	Mouth
12	D. K.	61	Myocardial degeneration; auricular fibrillation	Before After After	February 21 February 23 February 28	80 64 60	+4.0	1,580 1,580 1,790	14.0 15.0 14.0	+1.0 0.0	20.0 25.0 21.0	+5.0 +1.0	Tr. dig. 20 cc.	Mouth
13	L. S.	39	Rheumatic heart disease; mitral stenosis and insuffi-ciency	Before After	March 16 March 17	62 55	−5.0 −4.5	2,730 2,730	13.5 10.0	−3.5	15.0 22.0	+7.0	Tr. dig. 14 cc.	Mouth
14	S. C.	26	Rheumatic heart disease; pan-carditis with auricular fibril-lation	Before After	December 7 December 7	76 62	+10.0 +8.5	1,690 1,590	9.5 15.5	+6.0	19.0 26.0	+7.0	Stroph. 0.8 mgm.	Vein

while patients 1, 2, 3, 4, 5, 6, 12 and 13 showed signs of congestive failure of the circulation even when at rest. Patients 8, 12 and 14 exhibited fibrillation of the auricles, while in the other patients the rhythm was regular. In order to differentiate between the effect of rest and of digitalis, all patients were kept in bed for from 8 to 30 days, until clinical observations, electrocardiographic measurements, and tests of the vital capacity indicated no further improvement. Tested tincture of digitalis or strophanthin was then administered in large therapeutic doses. The effects of full digitalization were evidenced within 24 hours after beginning the administration of the drug. Circulatory measurements were then repeated within 24 hours after the administration of the last dose in all cases with the exception of patient 6, in whom the measurements were repeated 2 days after the last dose. All patients showed one or more effects of digitalization, such as slowing of the pulse rate, inversion of the T waves in the leads of the electrocardiographic tracings, or the appearance of nausea. Several patients showed several of these effects. As the main interest in this study was to observe the effect of the digitalis bodies on the pulmonary blood flow, which is closely related to the state of the entire body, the data for the patients are grouped in table 2 according to the degree of change in the pulmonary circulation rate following the administration of tincture of digitalis or strophanthin. Patient 1 showed the most marked decrease, and patient 14 the most marked increase of the pulmonary circulation time. The results indicate that only three patients (12, 13, and 14) of the fourteen patients studied showed a definite slowing of the pulmonary blood flow. In one of these three patients (number 12) six days after the beginning of the administration of digitalis the velocity was the same as before. In the other eleven patients the velocity of pulmonary blood flow was either unaltered or there was a definite increase as the result of the administration of the digitalis bodies. Accepting 3.5 seconds as the maximum normal variation, as was shown by the measurements on normal subjects, seven of the fourteen patients showed a definite increase above normal. The average increase in these seven patients was 6.9 seconds. The findings indicate no relationship between the changes in the velocity of pulmonary blood flow and that of the venous blood flow from the arm

to the heart. The vital capacities of the lungs showed no definite changes after the administration of digitalis. The venous pressure became definitely lowered in patients 1 and 4. No relationship could be established between the severity of circulatory failure and changes in velocity. The pulse rate was lower in all the patients with the exception of patients 2 and 9. The average slowing of the cardiac rate was 12 per minute (from 81 beats to 69). Definite correlation could not be established between the degree of circulatory failure and change in the pulmonary circulation time, although six of the seven patients who reacted with a definite increase in velocity showed symptoms and signs of congestive failure at the time of test. These patients were numbers 1, 2, 3, 4, 5 and 6. It is of interest to note that two of the three patients who exhibited fibrillation of the auricles showed definite prolongation of the pulmonary circulation time after the administration of large therapeutic doses of tincture of digitalis. These were patients 12 and 14. Patient 8, however, showed a decrease of 3.5 seconds.

DISCUSSION

The results of this study indicate that tincture of digitalis and strophanthin, and thus presumably other digitalis bodies, when administered to normal subjects under the conditions described, exert no appreciable change on the velocity of the pulmonary blood flow. When digitalis and strophanthin were administered to patients with cardiovascular disease the velocity of flow in the pulmonary circuit became distinctly slower in three patients, while in the rest of the eleven patients there was either no change, or a definite increase. The observations also indicate that following the administration of digitalis changes are greater in cardiac patients than in normal subjects.

Our observations in the past (7) (11) demonstrated that in circulatory failure there is slowing of the velocity of blood flow. Although slowing is not always proportional to the degree of clinical decompensation, with clinical improvement there is nevertheless generally an increase in the velocity of blood flow. The cardiac output of the heart in circulatory failure is not definitely known at present because of technical difficulties connected with the measurements. The conception expressed by certain investigators that with circulatory failure

there is an increase in the cardiac output could be reconciled with the findings of slowing of the pulmonary velocity only if one assumes that in cardiac failure there is considerable increase in the available cross sectional area of the vascular bed. At present experimental or clinical data are not available which throw light on this aspect of the problem. Similarly, no direct reliable observation on patients with circulatory failure is available which supports the theory that the beneficial effect of digitalis on the circulation manifests itself in a sedative action, decreasing the minute volume output of the heart. Our finding that seven out of fourteen patients with circulatory failure showed an increase in the velocity of blood flow in the pulmonary circuit following the administration of digitalis, is in harmony with other numerous observations on patients, in whom during their stay in hospital repeated measurements of the velocity of blood flow were taken. According to these observations, with improvement in the general clinical condition of the patient, the velocity of blood flow and the vital capacity increased and the venous pressure became lower.

The change in velocity of the blood flow following the administration of digitalis is therefore the same as the change which follows other therapeutic measures, which are beneficial in the treatment of circulatory failure. The observation that those patients who showed clinical improvement after the administration of digitalis bodies showed likewise an increase in the velocity of blood flow is of greater significance in the analysis of digitalis effect in patients, than finding no change or slowing. To condemn the use of digitalis because it fails to improve the circulation in a few patients is as irrational as giving up arsenicals because they do not always better patients with syphilis. It is often observed clinically that, depending probably on structural and physiological changes in the heart, a stage is reached when digitalis fails to benefit. In rare instances the symptoms and signs of circulatory failure may become definitely worse after the administration of digitalis and improvement may follow the omission of the drug. Our observations suggest that the digitalis bodies do not induce uniform changes in the velocity of blood flow of patients suffering from circulatory failure. This is in harmony with the findings of others on the effect of digitalis on the minute volume output of the heart, as well as on the cardiac rate, conducting

system, and vital capacity. If we consider that the degree as well as the nature of pathological changes in the structures through which digitalis influences the circulation vary markedly from patient to patient, it is questionable whether a uniform change in circulatory measurements after the administration of digitalis bodies can be expected.

The fact that seven patients showed definite increase in the velocity of pulmonary blood flow indicates that the digitalis bodies are useful agents in the treatment of circulatory failure. Since the relatively direct approach to the problem of the action of digitalis in patients with circulatory failure entails a number of variables it can be readily understood how hazardous is the application of observations gained in studying animals, or normal men.

SUMMARY AND CONCLUSIONS

1. Strophanthin and tincture of digitalis were administered intravenously and by mouth respectively to eight normal persons. Their effect on the velocity of pulmonary and peripheral venous blood flow, on the vital capacities of the lungs and arterial and venous pressures, were observed. Amounts of these drugs corresponding to large therapeutic doses failed to change appreciably the velocity of the pulmonary blood flow and the other above mentioned aspects of the circulation in the normal subjects.

2. When strophanthin, or tincture of digitalis in large therapeutic doses was administered to 14 patients suffering from cardiovascular disease, the velocity of the pulmonary blood flow became increased in seven, was unaltered in four, while in three patients it was definitely decreased.

3. Although the average pulse rate in seven patients showed a reduction of 14 beats per minute, the pulmonary circulation time showed an average reduction of 6.9 seconds, which corresponds to an increase of 30 per cent in the velocity of pulmonary blood flow.

4. The velocity of blood flow in the pulmonary circuit is decreased in patients with circulatory failure. With clinical signs of improvement due to the administration of digitalis or to rest the velocity of this blood flow increases, although the degree of the patient's improvement and the change in velocity may not be parallel.

5. Patients with symptoms and signs of congestive failure, even when at rest, have had a greater tendency to show definite increase in the velocity of blood flow in the pulmonary circuit following the administration of digitalis than patients who were compensated at rest.

6. The studies presented help to provide a rational basis for the therapeutic administration of digitalis to patients suffering from circulatory failure.

ABSTRACTS OF HISTORIES AND PHYSICAL EXAMINATIONS OF PATIENTS STUDIED

1. J. M., aged 62, complained of increasing dyspnea of one and a half years' duration. For three months he had been unable to walk because of marked weakness. He noticed marked swelling of the abdomen and legs. He was cyanotic and dyspneic. The heart was moderately enlarged. The sounds were distant. The cardiac rate per minute was 130 to 140. The rhythm was regular. The blood pressure was 120 mm. systolic and 50 mm. diastolic of mercury. Over the base of the lungs moist bubbling râles were heard. The abdomen was distended. The liver edge was felt 5 cm. below the costal margin. Marked pitting edema was noted over the buttocks and legs. The condition of the patient was unaltered at the time of the administration of digitalis. The diagnosis of myocardial degeneration was made.

2. J. C., aged 57, complained of shortness of breath and inability to work for one and a half years. He noticed swelling of the feet following exertion. The heart was normal in size. The cardiac rate was rapid. The sounds were distant. No murmurs were heard. At time of the administration of the digitalis bodies the patient was slightly dyspneic. The diagnosis of myocardial degeneration was made.

3. P. F., aged 63, was suffering from nocturnal attacks of dyspnea. During the last two years he had become weak and unable to work. Occasionally he noticed swelling of the ankles. On physical examination the heart was enlarged, the greatest diameter being 14 cm., and the aortic second sound was markedly accentuated. The rhythm was regular. Slight pitting edema was noticed over the ankles. The blood pressure was 210 mm. of systolic and 120 mm. diastolic of mercury. The patient's condition was unchanged at the time of the administration of digitalis. The diagnosis of arterial hypertension was made.

4. C. B., aged 41, complained of shortness of breath and weakness for one year. He noticed gradually increasing swelling of the ankles and legs during the six months previous to his entry to hospital. He was unable to walk during the same period. On physical examination he showed marked dyspnea and orthopnea. The lips were cyanotic. The heart was large. The greatest transverse diameter was 13 cm. The heart sounds were normal, and no murmur was heard. The

rate was rapid, 110 to 130. The rhythm was regular. There was marked swelling of the abdomen with a suggestive fluid wave. The liver area was tender. The legs were swollen with marked pitting edema. The blood pressure was 195 mm. systolic and 160 mm. diastolic of mercury. The patient's condition did not improve under rest in bed, and the symptoms and signs of circulatory failure were unchanged at the time of administration of digitalis. The diagnosis of arterial hypertension was made.

5. Th. J., aged 52, had been well until fourteen months previous to his entrance into the hospital, when he noticed cramp-like pain starting in the precordium and radiating to the epigastrium. This attack was repeated several times, he became very dyspneic on such occasions. During the last four weeks he noticed marked swelling of the ankles, which disappeared after rest. During the last two weeks he also coughed a great deal and has had several attacks of palpitation. The apex impulse was observed in the sixth interspace. The first sound at apex was short and merged into a soft systolic murmur. The second sound was reduplicated all over the precordium. The cardiac rhythm was regular. The peripheral vessels were sclerosed. A moderate degree of edema was observed over both ankles at the time of entrance into the hospital. The blood pressure was 140 mm. systolic and 100 mm. diastolic of mercury. At the time of test the general condition of the patient was the same, except that no edema was observed. The diagnosis of arteriosclerotic heart disease was made.

6. P. M., aged 50, noticed one month previous to his entry increasing shortness of breath, cough, swelling of the legs and abdomen. He was unable to work. On physical examination he was markedly orthopneic. The apex of the heart was not felt. The heart sounds were distant. The cardiac rate was rapid and the rhythm regular. The blood pressure was 155 mm. systolic and 80 mm. diastolic of mercury. The right side of the chest posteriorly was flat on percussion and the breath sounds were suppressed. Moist bubbling râles were heard over the base on both sides. The abdomen was tender over the liver area and it was large. The legs were markedly swollen. The condition was essentially unchanged at the time of administration of digitalis. The diagnosis of myocardial degeneration was made.

7. A. S., aged 74, complained of frequent attacks of precordial pain, associated with dyspnea. No other evidence of circulatory failure was obtained from the history. On physical examination some tortuosity and sclerosis of the retinal vessels were observed. The lips were cyanotic. The heart was of normal size. The heart sounds were weak but regular. The peripheral vessels were markedly thickened. The blood pressure was 190 mm. systolic and 95 mm. diastolic of mercury. Numerous moist rales were heard over the bases of the lungs. The diagnosis of arteriosclerotic heart disease and arterial hypertension was made.

8. P. P., aged 68, complained of shortness of breath and weakness. He had noticed swelling of the feet frequently after work. On physical examination the heart was found enlarged. The maximum of the transverse diameter was 13 cm.

The sounds were rather distant. The rhythm was totally irregular. The peripheral vessels were moderately sclerosed. The blood pressure was 120 mm. systolic and 70 mm. diastolic of mercury. No edema was noted. The condition of the patient at the time of test was essentially unchanged. The diagnosis of arteriosclerosis and auricular fibrillation was made.

9. W. M., aged 65, had had shortness of breath during the last six months previous to his admission. Two weeks previous to entry he noticed sharp abdominal pains which became aggravated after meals. He never observed swelling of the ankles, or of the abdomen. Physical examination showed an enlarged heart with a maximum transverse diameter of 14 cm. The heart sounds were of good quality and the pulmonary second sound was accentuated. Over the third right intercostal space a rough systolic murmur and a prolonged blowing diastolic murmur were heard. The peripheral vessels were moderately thickened. The pulses were full and bounding. Blood pressure was 196 mm. systolic and 50 mm. diastolic of mercury. No pitting edema or other signs of congestive cardiac failure observed. The Wassermann test of the blood was positive. The diagnosis of syphilitic heart disease with aortic insufficiency was made.

10. A. O., aged 68, gave no history of circulatory failure. He had been told that his blood pressure was high. The heart was slightly enlarged. The greatest transverse diameter was 12 cm. on percussion. The aortic second sound was markedly accentuated. The blood pressure was 228 mm. systolic and 112 mm. of diastolic. The diagnosis of arterial hypertension was made.

11. W. P., aged 39, suffered from attacks of precordial pain of two years' duration. During the last three weeks he had been suffering from shortness of breath which was worse at night. He also coughed a great deal during the same period. He had had no edema of the ankles despite the fact that he walked much. Physical examination showed marked pulsation of the vessels of the neck, over which a systolic murmur was heard. The apex impulse of the heart was felt in the sixth intercostal space in the anterior axillary line. The heart was enlarged downward and outward. The sounds were of good quality, with regular rhythm. Loud to and fro murmur was heard over the precordium with the maximum intensity over the aortic area. The radial pulses were of the Corrigan type. The blood pressure was 164 mm. systolic and 40 mm. diastolic of mercury. The Wassermann and Kahn tests of the blood were positive. The patient's condition was the same as just described at the time of the test. The diagnosis of syphilitic heart disease with aortic insufficiency was made.

12. D. K., aged 61, had had shortness of breath on exertion for one year. One month previous to his admission he became so weak that he could walk short distances only. No history of edema was obtained. The complaints were essentially the same as at the time of test. On physical examination the cardiac impulse was rather diffuse. The maximum transverse diameter was 13 cm. The sounds were of fairly good quality. At the apex a soft systolic murmur was heard. The rhythm was totally irregular. The peripheral vessels showed

moderate thickening. The blood pressure was 110 mm. systolic and 70 mm. diastolic of mercury. The liver edge was 3 cm. below the costal border. The diagnosis of arteriosclerotic heart disease and auricular fibrillation was made.

13. L. S., aged 39, was suffering from severe attacks of rheumatic fever at the age of 18. For one year he had noticed shortness of breath on exertion, as well as occasional swelling of the ankles. He was slightly dyspneic. The heart was slightly enlarged, the greatest transverse diameter being 12 cm. The first sound over the apex was loud. Over the same area a systolic and diastolic murmur was heard. The rhythm was regular. The liver was not palpated. Slight pitting edema over the ankles was noted. The blood pressure was 108 mm. systolic and 60 mm. diastolic of mercury. Under rest the patient improved and at the time of administration of digitalis he was not dyspneic and no edema was present. The diagnosis of rheumatic heart disease with mitral stenosis and insufficiency was made.

14. S. C., aged 26, complained of shortness of breath. He had had rheumatic fever in childhood but had been well until nine years previously, when, after pneumonia, he developed moderate shortness of breath for eight months. During the ten months before entry he experienced slight precordial pain on exertion with shortness of breath and palpitation, which gradually increased in severity forcing him to enter the hospital. Three days before admission, pitting edema was observed over lower legs. After admission to the hospital, on rest in bed and on taking digitalis, he showed moderate improvement. Physical examination showed blowing systolic and diastolic murmurs over aortic and mitral areas. The liver was not palpable. There was no edema of the legs. A few moist râles were heard over the left base. Following rest in hospital patient returned home but was compelled to re-enter hospital because of exacerbation of symptoms. At time of administration of strophanthin patient was up and about the ward. There was no dyspnea or orthopnea. Physical examination showed no râles over chest and no edema. The liver was not palpable, and the heart was as noted above. The diagnosis was rheumatic pericarditis; auricular fibrillation; aortic stenosis and insufficiency; mitral stenosis and insufficiency.

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