obtained from patients suffering from clinical typhus fever[6] some of which have been preserved by the lyophile process. Any serum showing anticomplementary action was treated by the method of Faran.[7] It was found that all except one gave positive reaction to both antigens, with titres mostly above 1:320, and one reaching as high as 1:20,480. Among these, 5 sera showed the same titre for both antigens, while 14 sera from 10 patients showed a higher titre to the epidemic antigen: 4 with a 2-fold difference, 4 with 4-fold difference, 5 with 8-fold difference and one positive only to epidemic antigen at titre 1:640.

Comment. The results of the present study by means of complement fixation test agree with a similar study, carried out by one of us (N.C.C.) in the spring of 1946 when epidemic and murine vaccines served as antigens. In that study, 9 patients with 15 samples of sera gave clear cut positive complement fixation reaction with one or both of the antigens. Seven patients with 10 sera gave stronger reaction to the epidemic, one gave equal titre, while another one gave higher titre to the murine antigen. These findings seem to suggest that the strains of rickettsia causing human infections in the past 2 years, whether in the autumn or in the spring, are largely of the epidemic type. This is in contrast to our previous results when the biological study of the organisms tended to classify them as murine type. In order to reconcile the above differences, further study will be made with perhaps absorbed sera. These will be continued when sera from fresh typhus cases will be available.

[6] We are indebted to Dr. Y. W. Yih, of the Hospital of the National Pei Ta Medical School for 4 of the sera tested.

[7] Faran, A., *J. Lac. Clin. Med.*, 1946, **31**, 1037.

[8] Bengtson, I. A., *Pub. Health Rep.*, 1947, **61**, 1379.

16605

Isometric Relaxation Period of the Left Ventricle in Normal Subjects and Patients with Mitral Stenosis.

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Differentiation of a split second sound from reduplication of this sound is important; the latter is consequent to loud snapping of the mitral leaflets in mitral stenosis while the former has a variety of causes, the most common of which is asynchronous closure of the aortic and pulmonic valves. Important information bearing on this problem may be afforded by study of the duration of the period of isometric relaxation of the left ventricle, for this period is the interval between closure of the aortic valve and opening of the mitral. Several attempts have been made to measure this period in normal subjects by means of arterial and venous tracings[1] or by observation of roentgenological tracings (electrokymograms).[2] The phonocardiogram has been used, thus far, for measuring this interval only in patients with mitral stenosis.[3] Errors due to delay in the transmission of the *v* wave from the right heart to the neck or asynchronism between right and left ventricles cannot be avoided in studies based on mechanical methods; similarly, inaccuracies due to the influence of position and motion phenomena may be present in roentgenological tracings. However, the phonocardiogram gives a virtually instantaneous recording of the vibration due to valvular movements and is

[1] Burstein, J., *Am. J. Phys.*, 1923, **65**, 158.

[2] Randak, E. F., Boone, B. R., Ellinger, G. E., and Oppenheimer, M. J., *Fed. Proc.*, 1948, **7**, 97.

[3] Margolies, A., and Wolferth, C., *Am. Heart J.*, 1932, **7**, 443.

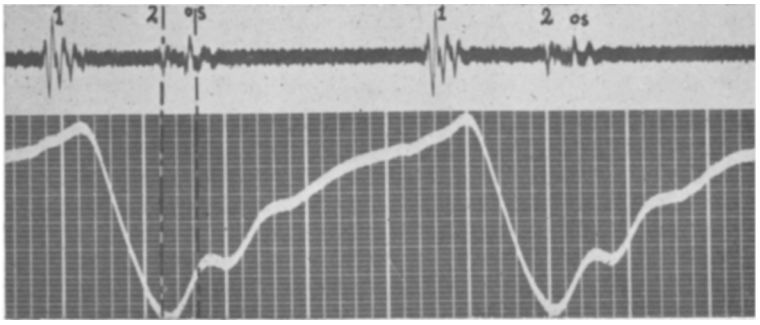

FIG. 1.
Simultaneous phonocardiogram and fluorocardiogram in a normal subject. The former has two vibrations indicating the closing of the semilunar valves (2) and the opening of the mitral valve (os). Between them lies the isometric relaxation period.

independent of other causes of error; it is therefore, the most accurate method. Thus far, only data obtained in cases of mitral stenosis are available[3] because, even if recognition of the various components of the second sound is often possible,[4] the vibration due to opening of the mitral valve can be recognized only in a small number of normal subjects. However, the systematic study of a series of over 1500 phonocardiograms collected by one of us (Luisada) showed the possibility of clearly isolating the vibration due to the opening of the mitral valve in a small percentage of cases. This vibration will be called "opening sound of the mitral valve".

Materials and Methods. This study is based on the above mentioned collection of phonocardiograms as well as the collection of fluorocardiograms and phonocardiograms of the Beth Israel Hospital. The records of seven normal subjects permitted measurement of the isometric relaxation period of the heart on the basis of the phonocardiogram. One of these cases also had a fluorocardiogram (electrokymogram) recorded and, therefore, permitted the analysis of the latter tracing on the basis of the phonocardiographic study (Fig. 1). Twenty-four cases had mitral stenosis with an evident opening snap of the mitral valve. This permitted the determination of the isometric relaxation period of the left ventricle in rheumatic heart disease where there is a possibility of delayed opening of the left auricular-ventricular valve. Parallel studies were made in 9 cases of mitral stenosis with a split second sound at the base, in 19 subjects having a similar splitting without mitral stenosis, and in 20 cases with a third heart sound. The phonocardiograms were recorded by means of a Sanborn "Stethocardiette", using a stethoscopic microphone with a 3.7 cm funnel applied at the apex, at the third left interspace, and at the second left interspace. The fluorocardiogram is a tracing of the movements of the cardiovascular fluoroscopic silhouette recorded by a phototube and a galvanometer. Details of this method have been given pre-

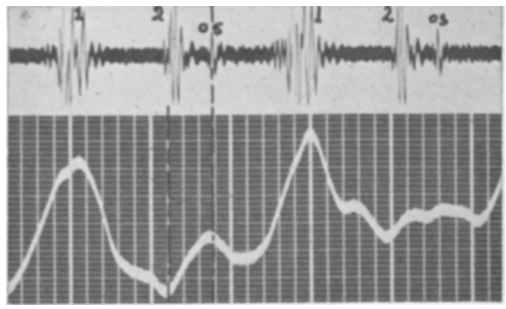

FIG. 2.
Simultaneous phonocardiogram and fluorocardiogram of a patient with mitral stenosis and auricular fibrillation. The sound tracing presents a loud opening snap of the mitral valve (os). Between the main vibration of the second sound (2) and the opening snap (os) is the isometric relaxation period which is prolonged.

[4] Rappaport, M. B., and Sprague, H. B., *Am. Heart J.*, 1942, **23**, 591.

TABLE I.

	Distance between main phase of 2nd sound and opening sound (or snap) of the mitral valve		Distance between the two phases of the split 2nd sound	Distance between 2nd and 3rd sounds
	Normal subjects	Mitral stenosis		
Maximum	0.07	0.11	0.05	0.18
Minimum	0.04	0.07	0.025	0.12
Average	0.055	0.079	0.04	0.15

viously.[5,6,7] In our collection of fluorocardiograms, 32 tracings were recorded in patients with mitral stenosis; one of the latter had a pronounced snap of the mitral valve (Fig. 2).

Results. The results are presented in Table I, in seconds.

The normal subject presenting a visible opening sound in the phonocardiogram, on whom a fluorocardiogram was recorded, showed the following:

(a) The interval between the main vibration of the second sound and the opening sound was 0.07 seconds.

(b) The tracing of the ventricle exhibited an early diastolic rebound.

(c) While the negative peak of the ventricular tracing coincided with the main vibration of the second sound, the opening sound coincided with the end of the initial rise and preceded the rebound (Fig. 1). Similar findings were present in tracings recorded along the left ventricular margin.

The patient with mitral stenosis and an opening snap of the mitral valve on whom a fluorocardiogram was recorded showed the following:

(a) The interval between main vibration of the second sound and opening snap was 0.11 second.

(b) The tracing of the left ventricle presented an early diastolic rebound.

(c) The relationship between opening snap and rebound is identical with that of the normal subject in spite of the prolongation of the isometric relaxation period.

Discussion. Our average figures for the duration of isometric relaxation in normal subjects are somewhat less than those found by Burstein.[1] This can be explained by the greater accuracy of our method which excluded transmission time of mechanical waves from the heart to the neck and results of phenomena taking place in both ventricles; moreover, our data were obtained by the use of a speed film. On the other hand, our findings coincided with those reported by Hoff.[8] Our data concerning measurements in patients with mitral stenosis are similar to those of Margolies and Wolferth[3] in regard to the average figures. Their minimum and maximum figures are respectively smaller and larger than ours, but they were found during extreme alterations of the cardiac rate. Our data on the interval between the two phases of a split second sound are shorter than those of Wolferth,[9] possibly because of a different choice of cases, while those concerning the third sound are identical with his. There is a slight difference between our data concerning the third sound and those of Rappaport and Sprague.[4] This difference can be explained by the fact that these authors measured the interval from the beginning of the second sound.

Simultaneous observation of the phono-

5 Luisada, A. A., Fleischner, F. G., and Rappaport, M. B., *Am. Heart J.*, 1948, **35**, 336 and 348.

6 Luisada, A. A., and Fleischner, F. G., PROC. SOC. EXP. BIOL. AND MED., 1947, **66**, 436.

7 Fleischner, F. G., Romano, F. J., and Luisada, A. A., PROC. SOC. EXP. BIOL. AND MED., 1948, **67**, 535.

8 Hoff, H. E. Events of Cardiac Cycle. In Howell's Textbook of Physiology by Fulton, Saunders, Philadelphia. 1946.

9 Wolferth, C. C. Heart Sounds, in Cyclopedia of Medicine, Vol. 3. F. A. Davis, Philadelphia.

cardiogram and fluorocardiogram, both in the case with a physiological opening sound and in that with a pathological opening snap, indicates the following:

The part of the fluorocardiogram which corresponds to the isometric relaxation period

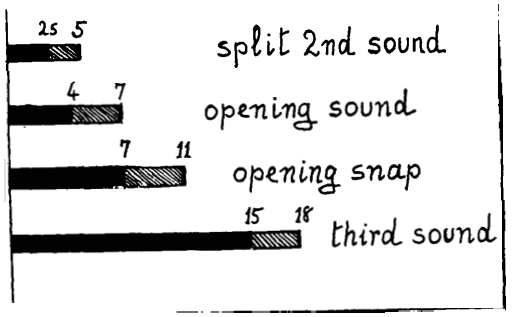

FIG. 3.
Scheme indicating the distance in hundreds of seconds between the two phases of a split or reduplicated second sound and between second sound and third sound. The black bar indicates the minimal distance, the striped bar, the maximal distance between the two phases of the reduplicated sound or between second and third sound. *Split second sound,* recorded over the pulmonic area. *Opening sound,* recorded over the mitral area in normal subjects. *Opening snap,* recorded over the apex or mitral area in patients with mitral stenosis. *Third sound,* recorded over the apex in normal subjects.

lies between the lowest point of the ventricular wave and the beginning of the rebound, and not that ending with the lowest point of the rebound, as suggested by others.[10] However, this period cannot be measured routinely on the various fluorocardiographic records because the diastolic rebound is not a constant feature; it may be represented by a less steep rise of the tracing or may be completely absent. According to our data, the figures found recently by others[2] for the isometric relaxation period are too long, especially because they did not study patients with mitral stenosis; as known, these may present the longest duration of the isometric relaxation period because of impaired opening of the mitral valve.

The results of our study, sketched in Fig. 3, facilitate basing the classification of an extra-sound on the above temporal data.

Summary. The isometric relaxation period of the left ventricle in normal subjects and in patients with mitral stenosis was studied. This period was measured on the phonocardiogram as the interval between the main vibration of the second sound and the opening sound or snap of the mitral valve.

The findings in 7 normal subjects varied between 0.04 and 0.07 seconds; 24 mitral patients had figures of from 0.07 to 0.11 seconds. Additional data on the split second pulmonic sound and the third heart sound are presented.

Simultaneous phonocardiograms and fluorocardiograms in a normal subject and in a patient with mitral stenosis, both having an opening sound or snap of the mitral valve, allowed correlation of the ventricular fluorocardiogram with the sound tracing in regard to the isometric relaxation period.

[10] Boone, B. R., Chamberlain, W. E., Gillick, F. G., Henny, G. C., and Oppenheimer, M. J., *Am. Heart J.*, 1947, **34**, 560.

16606

Staphylococcus aureus: Drug-fastness Studies with Penicillin and Sulfactin.*†

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Sulfactin, a new antibiotic produced by an Actinomyces, was described by Junowicz-Kocholaty, Kocholaty, and Kelner.[1] Its bacterial spectrum, toxicity, and therapeutic action in mice were described by Morton.[2] It was found that there was a very favorable ratio between