

ergotoxine eliminated the hyperthermic effect. Subcutaneous administration of ergotoxine gave rise to less dramatic hyperthermic responses and to hypothermia (in cold environments) that was essentially the same as that

elicited by intraperitoneal injection.

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The Changes in the Electrocardiogram Associated with Standing.*

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Differences of opinions concerning the mechanism for the changes in the electrocardiogram that occur with standing are great. They are mainly due to the fact that some investigators were exclusively interested in the alterations which appeared immediately after assuming the erect position while others studied only those changes which occurred after minutes of standing. There is agreement that the *immediate* changes are due both to the change of the position of the heart and to an altered contact between the heart and the neighboring structures which show different conductivity.^{1,2,3} The alterations which appear later, *viz.*, during continued standing are attributed by some authors to an altered blood supply to the heart,⁴ while others assume a change in the tonus of the sympathetic nervous system which modifies the repolarization processes in the heart. This latter contention is based chiefly on the finding that after administration of sympathicolytic

drugs positional changes failed to appear in the electrocardiogram.^{5,6}

We studied this problem on 80 male patients who had no evidence of organic heart disease. Electrocardiograms were taken with the patient in the supine position, immediately upon standing, after standing for 1 minute, 5 minutes, 15 minutes and again immediately upon lying supine. In 12 patients 0.5 mg of Dihydro-ergotamine 45 was given intravenously and records were again taken in the supine position at the height of the systemic effects and on standing.

Results. Of the 80 patients, 25 or 31.2% showed significant electrocardiographic changes on standing. Some of the changes occurred immediately upon standing while others took place many minutes after standing was maintained.

Fig. 1 and Fig. 2 show that the final deflection in the electrocardiogram may become higher or lower with prolonged standing. Changes may appear immediately, disappear later and reappear (Fig. 1) or they may be absent immediately on standing, but appear later (Fig. 2).

A further significant result of our studies was the temporary appearance of A-V rhythm with a change of position in 4 cases (Fig. 3) and the frequent appearance of a marked sinus arrhythmia.

Finally, the studies revealed that in 11 out of 12 cases the significant electrocardio-

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¹ Sigler, L. H., *Am. Heart J.*, 1938, **15**, 146.

² Scherf, D., and Weissberg, J., *Am. J. M. Sc.*, 1941, **201**, 693.

³ White, P. D., Chamberlain, F. L., and Graybiel, A., *Brit. Heart J.*, 1941, **3**, 233.

⁴ Akesson, S., *Uppsala läkeref. förh.*, 1936, **41**, 383.

⁵ Nordenfelt, O., *Acta med. scand. Suppl.*, 1941, **119**, 1.

⁶ Wendkos, M. H., *Am. Heart J.*, 1944, **28**, 549.

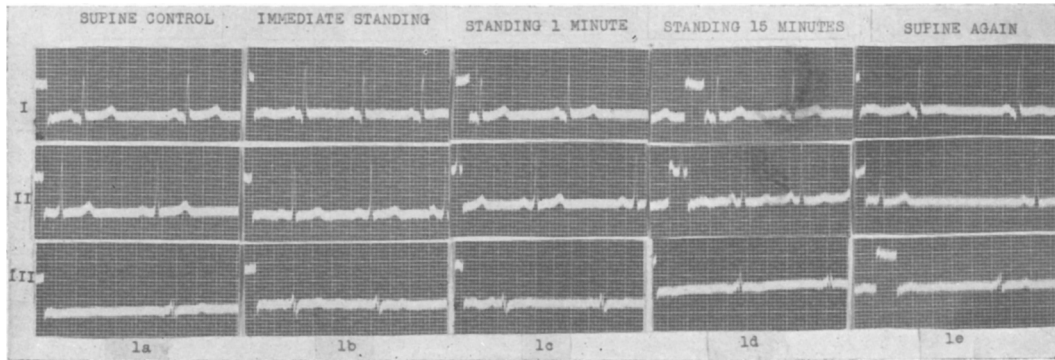


FIG. 1.

30-year-old healthy man; the changes which appeared immediately on standing disappeared within one minute; some alterations are again visible after standing for 15 minutes; on resumption of the supine position a marked bradycardia occurred and the electrocardiogram did not return to normal. Blood pressure varied between 105/70 and 120/70.

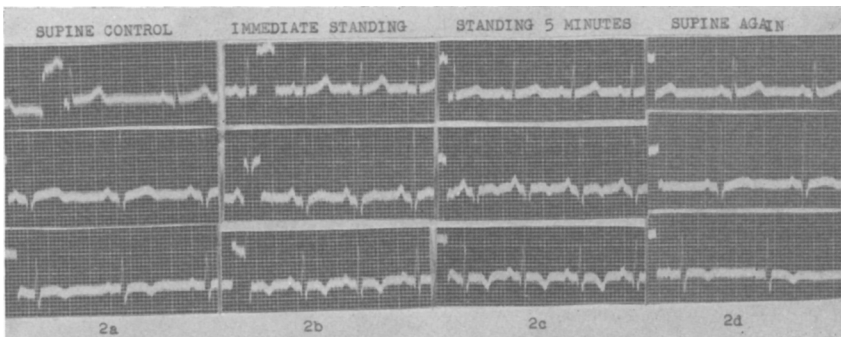


FIG. 2.

25-year-old man with early pulmonary tuberculosis; the alterations after standing for 5 minutes are more pronounced than those which appeared immediately on standing (lead II). On lying supine the blood pressure was 115/75, on standing it was 95/75.

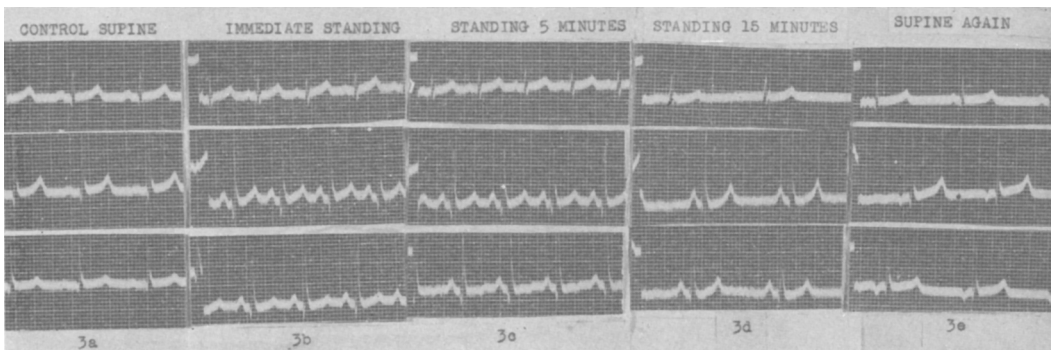


FIG. 3.

46-year-old man with early bronchogenic carcinoma. Changes appeared after 5 minutes of standing, and disappeared later (lead III); an A-V rhythm appeared after 15 minutes temporarily (lead I) and persisted for a few minutes on resumption of the supine position. No significant changes of blood pressure.

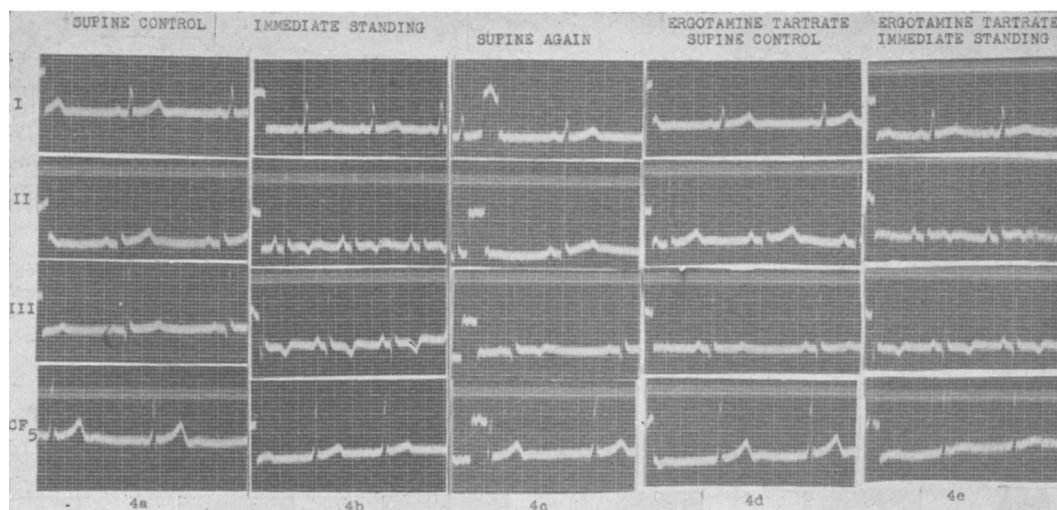


FIG. 4.

A 20-year-old man with intestinal parasites. Marked changes appear on standing and they remain uninfluenced by administration of ergotamine. No significant changes of blood pressure.

graphic changes which appeared immediately on standing could not be prevented by the administration of dihydro-ergotamine 45 (Fig. 4).

Comments. The *immediate* alterations of the electrocardiogram with changes of posture cannot be explained by an insufficient blood supply to the heart. In experiments in which the patients were tilted, it was shown that the changes appeared immediately when a certain angle was reached.⁷

The changes in the electrocardiogram caused by anoxia develop slowly within one or more minutes and also disappear gradually. The same argument holds for changes caused by a change in the tonus of the sympathetic nervous system.

Anoxia however, may be the explanation for those changes which occur during prolonged standing. Originally it was assumed⁴ that prolonged standing leads to an accumulation of blood in the lower part of the body and a consequent diminished blood supply to the heart (orthostatic anemia). Unusually marked alterations in the limb and chest leads with simultaneous anginal pain were described in a healthy 21-year-old individual when in the erect position.⁸ Against this

interpretation for the electrocardiographic changes is the fact that in such patients the blood pressure may remain normal on standing, while in others with marked orthostatic hypotension no electrocardiographic changes appear.⁵

Another mechanism however, seems possible. Without the activity of certain reflexes marked hypotension and fainting would appear in every individual on standing. It is entirely possible that in the course of the widespread reflex regulation of the arterial bed the coronary vessels are involved. Marked changes in the electrocardiogram are observed in patients suffering from an acute profuse hemorrhage. These patients need not show any fall of blood pressure nor an anemia, since the alterations are observed with a hemoglobin of 80%. It has been concluded that reflexes from the carotid sinus and the McDowall reflex lead to a readjustment of the arterial bed in which the coronary arteries participate.⁹ Thus reflex changes of the tonus of the autonomic nerves regulating the width of the coronary arteries in conjunction with the increased heart rate on standing may,

⁸ Akesson, S., *Acta med. Scand. Suppl.* 1947, **196**, 192.

⁹ Scherf, D., and Klotz, S. D., *Ann. int. Med.*, 1944, **20**, 438.

⁷ Mayerson, H. S., and Davis, W. D., *Am. Heart J.*, 1942, **24**, 593.

temporarily lead to varying degrees of anoxia of the heart muscle.

The changes in the tonus of the autonomic nerves (in mammals particularly the sympathetic nerves) which has been mentioned above can also directly influence the final deflection of the electrocardiogram. In favor of the presence of such changes in tonus is the appearance of A-V rhythm with changes in posture (Fig. 3) and the remarkable fact that pronounced abnormalities of the P-R interval disappear or diminish when the subject is erect.^{10,11,12} A change of the tonus of the sympathetic nervous system will modify the form of the T waves and the ventricular gradient. The sympathetic nerves accelerate the repolarization process. Under normal conditions the subendocardial layers are depolarized earlier and repolarized later than the subepicardial muscular layers. This is probably due to the high intraventricular pressure. A faster repolarization of the inner layers would lead to a depression and inversion of the T waves.

The importance of a change in the tonus of the sympathetic nervous system is demonstrated by the absence of positional electrocardiographic alterations after the administration of sympathicolytic drugs.^{5,6,13}

The frequent ineffectiveness of ergotamine shown in this report (Fig. 4) had to be expected, because the immediate changes appearing on standing are not due to a change of sympathetic tonus as frequently maintained. There is furthermore no proof that the sympathetic system alone is involved in the electrocardiographic changes which appear on continued standing.

Summary. The immediate alterations in the electrocardiogram caused by assuming the erect posture and those appearing during standing, were studied in 80 patients.

The genesis of the changes which appear immediately on standing and disappear immediately when the supine posture is resumed is separated from those which are seen during prolonged standing. The latter is ascribed to changes in the tonus of the autonomic nervous system which may act on the heart muscle directly or via the coronary arteries.

A-V rhythm may appear on standing due to the change of the tonus of the autonomic nerves.

Administration of ergotamine preparations does not always prevent the appearance of immediate changes in the electrocardiogram on change of posture.

Our thanks are due to Dr. Henze of the Sandoz Drug Company for the supply of Dihydro-Ergotamine 45.

¹⁰ Poel, W., *Arch. int. Med.*, 1942, **69**, 1040.

¹¹ Holmes, J. H., and Weill, D. R., Jr., *Am. Heart J.*, 1945, **30**, 291.

¹² Manning, G. W., and Stewart, C. B., *Am. Heart J.*, 1945, **30**, 109.

¹³ Spuehler, O., *Schweiz. med. Wchschr.*, 1947, **77**, 28.

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A Comparison of the Acute Toxicity of Two Forms of Thiamine.*

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Recently there has become available for investigational use a new form of vitamin B₁,

thiamine mononitrate. Considering the wide therapeutic use and the parenteral toxicity of thiamine hydrochloride,¹⁻¹³ it was thought

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¹ Steinberg, C. L., *Am. J. Digestive Dis.*, 1938, **5**, 680.