for reticulocyte levels and red cell Fe^{59} incorporation showed that both increased as the dose was augmented, but reticulocyte response gave more variable results especially at lower dose levels in the transfused rats. This variability, thought to result from the method of reticulocyte counting, restricts use of this parameter to assay of relatively high doses of erythropoietin. Although measurement of red cell iron incorporation provided a simple and reliable means of measuring both high and low doses of erythropoietin, the amount of blood required for determination of Fe^{59} incorporation at the dose of radioiron employed precluded the use of a single animal for serial determinations.

The dose-response analyses in these experiments were similar to those of Garcia and Van Dyke(3) and Hodgson *et al.*(5) in that the relationship between the log of the dose of urine concentrate or plasma extract in milliliters and the erythropoietic response was linear. Schleuter *et al.*(12) found a sigmoid relationship between Fe^{59} incorporation in erythrocytes of starved rats and the log dose of purified erythropoietin obtained from anemic sheep plasma. Within the range tested in the present study a sigmoid dose-response relationship was not noted.

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Automatic Screening of Normal and Abnormal Electrocardiograms by Means of a Digital Electronic Computer.* (26260)

HUBERT V. PIPBERGER, ROBERT J. ARMS AND FRIEDEMANN W. STALLMANN
Veterans Administration Hospital, Mt. Alto, National Bureau of Standards, and Dept. of Medicine, Georgetown University School of Medicine, Washington, D.C.

In a digital computer program for automatic analysis of electrocardiograms (ECG) a screening procedure for separation of normal and abnormal records appears an essential preliminary step. A more detailed analysis of pathological tracings may then follow. Since the ECG consists of several distinct wave forms (P, QRS and T waves) with different electrophysiological significance a single screening procedure should preferably encompass analysis of all electrical processes which accompany each heart beat. The spatial ventricular gradient ($SV\hat{G}$) appeared as the most comprehensive single parameter known for this purpose.

Wilson *et al.*(1) developed the concept of $V\hat{G}$. It has been defined as the net electrical effect of the differences in time course of ventricular depolarization and repolarization. As predicted by simple theory, the time integral ($\hat{A}$) of depolarization potentials of a muscle should be equal to those of repolarization but with opposite sign. For the ECG, the sum of the time integrals of QRS and T should be

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zero. In most ECG leads from normal hearts, however, QRS and T have the same polarity and the sum of their time integrals has a finite value. From this Wilson *et al.*(1) concluded that in normal hearts a difference in the time course between depolarization and repolarization must exist. $\hat{VG}$ is an indicator of this difference ($\hat{A}$ QRS + $\hat{A}$ T = $\hat{VG}$).

Clinical application of $\hat{VG}$ has always been very limited because its determination by graphic means is very time-consuming. Furthermore, many investigators found a poor separation between normal and abnormal tracings when $\hat{VG}$ was determined in frontal plane projections only, as commonly done. To determine accurately the spatial characteristics of $\hat{VG}$ ($\hat{SVG}$), however, weighted ECG leads with a constant ratio between generated current strength and recorded potentials and with constant direction are required (2). Conventional bipolar and unipolar leads do not fulfill these requirements. The more recently developed corrected orthogonal lead systems(2) have been designed according to these needs. Schmitt's SVEC III leads (3) were used in the present study.

Material and methods. Corrected orthogonal electrocardiograms(3) were recorded on magnetic analog tape from 122 normal subjects and 144 randomly selected patients with ECG abnormalities. ECG preamplifiers together with FM (frequency modulation) record amplifiers of the tape recorder† gave a flat frequency response from 0.1 to 1,250 c.p.s. An automatic analog-to-digital data converter with a sampling rate of 1,000/sec. for each ECG lead was used to re-record the tracings on digital magnetic tape. The conversion method has been described previously (4). The digital format chosen was that of the IBM 704 computer which was used for the study. The base line for determination of time integrals was computed as a straight line between averages of 15 digits preceding the P-wave and following the T-wave. Time integrals were then obtained for the entire cardiac complex by subtraction of negative areas from positive ones (Fig. 1). The P-wave was included because the auricular gradient approaches zero and is, therefore, negligible.

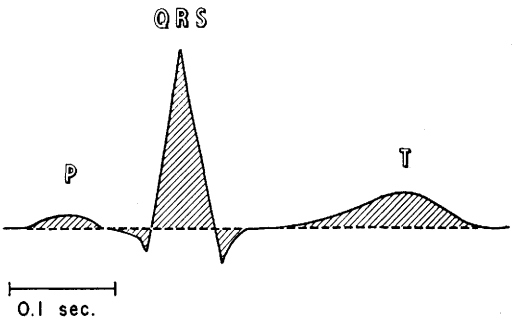

FIG. 1. Determination of ventricular gradient ($\hat{VG}$) in one orthogonal lead. The time integral of total complex (P, QRS and T) is obtained by subtraction of negative areas from positive ones. The same procedure is performed in all 3 orthogonal leads. Results expressed in mVsec. Spatial ventricular gradient ($\hat{SVG}$) is then constructed as a spatial vector on the basis of the 3 time integrals obtained from the 3 orthogonal leads.

Results. The following results were printed out by the computer: 1. $\hat{VG}$ for each orthogonal lead; 2. Spatial magnitude of $\hat{SVG}$ derived from the orthogonal components, expressed in mVsec.; 3. Spatial direction of $\hat{SVG}$ in spherical coordinates (azimuth and elevation angles).

The mean magnitude of $\hat{SVG}$ in the group of 122 normals was 0.123 $\pm$ 0.047 mVsec. The mean direction was leftward, inferiorly and anteriorly (as related to the body of subjects). Only a few normal subjects showed a slightly posterior direction of $\hat{SVG}$. Two standard deviations of the mean results were used for determination of normal ranges for magnitude and spatial direction. Six cases fell out of these ranges.

Consequently, $\hat{SVG}$ of the 144 abnormal records was compared with the normal standards. Results are given in Table I. The overall accuracy of the decision "normal" or "abnormal" was 91% when compared with conventional clinical interpretations of the standard 12-lead ECG and vectorcardiograms of these patients. In the category of old myocardial infarctions only 1 case out of 56

† Ampex Corp., Type FR 104.

TABLE I.

	No. of cases	Abnormal in direction	Abnormal in amplitude	Total No. recognized as abnormal
		%	%	%
Myocardial infarction (old)	56	53 (95)	24 (43)	55 (98)
Left ventricular hypertrophy	34	24 (71)	14 (41)	28 (82)
Right " "	14	9 (64)	6 (42)	10 (71)
Left ventricular conduction defect	19	18 (95)	10 (53)	19 (100)
Right " " "	21	16 (76)	12 (57)	19 (90)
Total	144	120 (83)	66 (46)	131 (91)

was not recognized as abnormal. The accuracy in recognition of cases with left or right ventricular hypertrophy was somewhat less, being 71 and 82% respectively. Directional discrepancies between normal and abnormal were considerably more significant than those of $S\hat{V}\hat{G}$ magnitude (Table I).

Discussion. In the described procedure, ECG recording and data processing is trusted completely to technicians and automatic equipment. The physician needs to read and interpret, therefore, only those records which are recognized by the computer as being abnormal. This automatic procedure lends itself, therefore, to large-scale epidemiological studies of coronary artery disease and other cardiac disorders.

The accuracy of the screening process was determined by comparison of the results with conventional interpretations of the standard 12-lead ECG and vectorcardiograms (VCG). Burch *et al.*(5) and Hugenholtz *et al.*(6) have found in autopsy correlations that the diagnostic accuracy in recognition of myocardial infarcts is enhanced when VCG is used in addition to ECG. Since both were used in the present study, it appears that the diagnostic accuracy of the automatic screening procedure is at least as high as or higher than that of the conventional 12-lead ECG alone.

Due to the small number of cases in some of the pathological subcategories, no attempt has been made to determine statistical ranges for these abnormal groups. Refinements of the described procedure may lead to grouping of cases according to specific ECG diagnoses.

Summary. The spatial ventricular gradient was determined in 256 electrocardiograms by means of a digital electronic computer. This automatic procedure allowed separation of normal and abnormal records with a high degree of precision. Of all cases with old myocardial infarctions, which are of prime interest in electrocardiographic diagnosis, 98% were recognized as abnormal.

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