Evolution of QRS-T Relationship From Birth to Adolescence in Frank-lead Orthogonal Electrocardiograms of 1492 Normal Children

P. M. Rautaharju, M.D., Ph.D., A. Davignon, M.D., F. Soumis, Ph.D., E. Boiselle, B.E., and A. Choquette

SUMMARY
Patterns of evolution of QRS-T relationship were investigated by determining statistical distributions of QRS and STT integral vectors and the ventricular gradient vector in 1492 normal children divided into 12 age groups from birth to the age of 16 years. From birth to the age of 4 days, the ventricular gradient vector shifts posteriorly and to the left due to posterior shift of the STT integral vector and an increase in the spatial angle between QRS and STT integral vectors to a mean value of 103°. These early neonatal changes in QRS-T relationship probably reflect the sudden reduction of hemodynamic load and the subsequent postnatal atrophy of the right ventricle while the left ventricular load slowly increases. The magnitude of the ventricular gradient vector increases from age 3 weeks until about 7 years. This increase appears to be related to a gradual increase in the magnitude of the QRS and STT integral vectors and a drastic decrease in the spatial angle between them. The spatial angle between QRS and STT integral vectors reaches its minimum (22°) in the age group 1.5-4.5 years, suggesting that at that age the average direction of ventricular excitation and repolarization wavefronts are nearly opposite to each other.

In addition to the shifting balance between the left and right ventricular hemodynamic load, other factors, such as the maturation of the sympathetic nervous system, may be important in determining spatial gradients in the duration of action potentials, thus influencing the relationship between ventricular excitation and repolarization.

THE RELATIVE RIGHT and left ventricular hemodynamic load undergoes profound alterations during early neonatal period, and then gradually changes during the postnatal phase. The growth and maturation periods during childhood and adolescence can also be expected to influence the hemodynamic load of both ventricles. These functional and structural organic changes in the heart and extracardiac tissues parallel substantial evolutionary changes in electrocardiographic (ECG) and vectorcardiographic (VCG) patterns of normal children. Guller et al.1 reported significant changes in several Frank-lead ECG measurements during the first 72 hours of life. Liebman et al.2-4 have extensively reported on changes with age for a large number of VCG measurements for McFee-Parungao and Frank lead systems. Borun et al.5 have reported on age changes in normal children for scalar amplitude measurements for Cube and Frank leads. The VCG changes reflect, in general, increasing relative dominance of the left ventricle with increasing age.

The investigators cited above have performed extensive statistical analyses on large numbers of Frank lead VCG variables. However, we know of no systematic analysis in the literature on the changes in the ventricular excitation-repolarization relationships with age in normal children. In this investigation we analyzed the patterns of evolution of normal QRS-T relationships from birth to age 16 years.

Methods and Study Groups
The study population was composed of 1492 Caucasian, Canadian children aged 0-16 years. This group is a subgroup of a larger population of children that formed the source material for the establishment of normal standards for the conventional 12-lead ECG.6 The age breakdown of the group is given in table 1. Included in the study were only those subjects in whom we could obtain both a good-quality 12-lead ECG and the Frank-lead ECG. Approximately equal numbers of boys and girls were studied. All children had a complete physical examination, and only those without clinical evidence of disease were included in the study. Newborns were recruited from a hospital with a large obstetrical service, and the other age groups were screened either from well child clinics or from primary and secondary schools in Montreal.

The conventional 12-lead ECG and the Frank-lead ECG were recorded simultaneously on magnetic tape (Ampex Model C-602 FM recorder). The Frank-lead ECG was recorded at the level of the fifth intercostal space, with electrodes C and A corresponding to the locations of V₄ and V₆. The recording system was coupled with a Marquette Model C-242 direct writing ECG console to permit visual quality check of the ECG tracing while it was recorded on magnetic tape. The recording was repeated, several times if necessary, until a satisfactory tracing was obtained.

Each subject was given an identification code which included age, weight, height and sex. Signal preprocessing was performed with an IBM 1800 com-
computer. Analog-to-digital conversion was performed with a sampling rate of 333 samples/sec per channel. Frank-lead ECG analysis was performed using a high-resolution wave detection and measurement program described elsewhere. Visual verification of all computer wave measurements was performed using an interactive computer graphics terminal which allowed us to correct occasional computer wave detection errors.

The study population was divided into 12 subgroups. We attempted to accumulate more records in younger age groups where the ECG changes take place relatively quickly. However, the age grouping was somewhat arbitrary in that we decided to avoid a breakdown into subgroups smaller than 100 children. The reason for this decision was the desirability to retain the standard error for the lower 2% and the higher 98% confidence limits for normal values within reasonable tolerance limits for practical applications, thus improving the stability of the 96% normal range.

The present report deals specifically with scalar and vector variables derived by integration of various segments of the ECG. The terminology we use defines three vector quantities. The QRS integral vector is obtained by integrating the X, Y and Z components from the beginning to the end of QRS; the STT integral vector is obtained similarly by integrating within the time window spanning from the end of QRS to the end of the T wave. The third vector quantity, the QRS-STT integral vector or the ventricular gradient vector, is defined as the vector sum of the QRS and STT integral vector. The integration constant is defined by a voltage reference (baseline) determined as the average potential in a 16-msec window preceding the beginning of QRS. A right-handed orthogonal Cartesian coordinate reference system is used, with positive X, Y and Z directions to the left, inferior and posterior, respectively.

### Results

Of special interest in studying ventricular excitation and repolarization is the relationship between QRS and STT integral vectors. Figures 1 and 2 show a convenient condensed display format to demonstrate age changes. This display summarizes the median distribution in each age group. The bivariate 50 percentile confidence limits calculated about the group mean values are depicted separately for horizontal and frontal plane projections of the integral vectors.

Figures 1A and B show that during the first 5 days of life the QRS integral vector is oriented to the right and anteriorly, indicating that excitation wavefronts in the right ventricle dominate in the delicate relative balance of the right and left ventricular excitation.

The QRS integral vector shows a distinct pattern of evolution with normal growth and maturation, with a gradual systematic counterclockwise shift and rotation in the horizontal plane from right-anterior to left-posterior. The magnitude of the QRS integral vector increases in the frontal plane, there is a slow, systematic shift to the left until about the age of 10 years.

Figures 2A and B show the median bivariate confidence limits for the QRS-STT or the ventricular gradient vectors. In the horizontal plane projection, the evolution of the ventricular gradient vectors follows a clockwise trajectory with a direction opposite to that of the evolution of the QRS integral vector. This observation suggests that the STT integral vector also evolves very differently from the QRS integral vector. This prediction is confirmed by figures 3A and B. An inspection of the bivariate distributions reveals that the STT integral vector is oriented to the left during the first 24 hours of life and shifts posteriorly with increasing magnitude during the first week of life. At about 1 week, the orientation of the STT integral vector in the horizontal plane is, on the average, nearly diametrically opposite to that of the QRS integral vector.

From 1 week on, the evolution of the STT integral vector in the horizontal plane takes place in the opposite direction from that of the QRS integral vector, with a clockwise shift and gradual increase in magnitude. In the frontal plane projection, the STT integral vector orientation changes remarkably little with age. A pronounced increase in the magnitude of the STT integral vector is noticed throughout the aging process from birth to 16 years of age.

Figures 4 and 5 give the confidence limits at 2, 5, 25, 50, 75, 95 and 98 percentile levels for the spatial magnitudes of the QRS and STT integral vectors.

A traditional electrocardiographic index of excitation-repolarization relationships is the total integral of QRS-ST-T, or various scalar components of the so-called ventricular gradient vector. Figure 6 shows the increase in the spatial magnitude of the ventricular gradient vector from a mean value 39 μV-sec at the age of 3 weeks to 103 μV-sec in the age group 10–12 years. After 12 years, the spatial magnitude of the ventricular gradient vector declines again, to 92 μV-sec in the age group 14–16 years. The spatial magnitude of the ventricular gradient vector appears to remain unchanged during the first 2–3 weeks of life.

Figure 7 indicates that the increase of the magnitude of the ventricular gradient vector with age
FIGURE 1. The evolution of QRS integral vector in normal children from birth to adolescence. The ellipses depict bivariate 50% confidence limits for frontal (A) and horizontal (B) plane projections in every second age group numbered from 1–11 according to age ranges given in table 1.

coincides with the drastic decrease of the spatial angle between QRS and STT integral vectors from the third week to about 4.5 years of age. In this age range, the increase of the spatial magnitude of the ventricular gradient vector appears to be determined primarily by the decreasing spatial angle between the QRS and STT integral vectors. The increasing magnitude of the QRS and STT integral vectors (figs. 4 and 5) contribute to the increase of the spatial magnitude of the ventricular gradient vector, and may be a dominant factor from age of 4.5 years until the age of 10–12 years.
Of special interest is the situation in the age group 1.5–4.5 years regarding the relationship of QRS and STT integral vectors. The mean spatial angle between these two vectors in this age group reaches its smallest value, 22°.

The direction of the QRS integral vector can be taken to indicate the mean general direction of ventricular excitation and that of the STT integral vector the reverse of the mean direction of ventricular repolarization. On that basis, it appears that at the age of 1.5–4.5 years the average direction of ventricular excitation fronts is to the left in the frontal plane, at an
angle of about 45° down from the horizontal plane, and that the direction of ventricular repolarization is on the average nearly opposite that of ventricular depolarization.

**Discussion**

Several ECG and VCG studies have demonstrated significant correlations between ECG and various
FIGURE 4. Percentile distributions for the spatial magnitude of the QRS integral vector in normal children from birth to age 16 years.

FIGURE 5. Percentile distributions for the spatial magnitude of the STT integral vector in normal children from birth to age 16 years.
FIGURE 6. Percentile distributions for the spatial magnitude of the ventricular gradient or QRS-STT integral vector in normal children from birth to age 16 years.

FIGURE 7. Percentile distributions for the spatial angle between the QRS and STT integral vectors in normal children from birth to age 16 years.
hemodynamic parameters in right, left or biventricular overload.\textsuperscript{5-8} The relative right and left ventricular hemodynamic load changes dramatically at birth and during early infancy, and is followed by a more gradual evolution of the left ventricular load during the growth and maturation period during childhood and adolescence. These functional and structural organic changes in the heart and extracardiac tissues parallel substantial evolutionary changes in ECG and VCG patterns of normal children.

Ellison et al.\textsuperscript{4} have demonstrated a high level of correlation between the maximum leftward dipole moment and the body weight in a group of normal subjects aged from 2 weeks to 28 years. Thus, the evolution of the QRS vectors probably reflects the normal growth of the heart. However, this observation does not explain the changes in QRS-T relationship.

The concordance of QRS and T and the speculated reasons for it has been controversial for several decades. Theoretical analysis by Burger\textsuperscript{45} more than 20 years ago reveals that the ventricular gradient is inherently related to the spatial gradients of durations of the excitatory state, i.e., spatial dispersion of action potential durations. Our results suggest that anatomic and functional hemodynamic changes associated with birth, growth and maturation of normal children may have a profound influence on the QRS-T relationships.

The initial increase of the spatial angle between the QRS and STT integral vectors during the first 5 days of life appears to be closely related to the posterior shift of the STT integral vector, while the QRS integral vector remains relatively unchanged. Associated with the posterior shift is the change of the polarity (from negative to positive) of the mean value of the T-wave amplitude in Z lead during the first 72 hours of life, as reported by Guller et al.\textsuperscript{1} These observations probably reflect the reduction of the pressure load of the right ventricle after birth and the subsequent postnatal atrophy of the right ventricular wall. During the first month of life, the left ventricular weight increases much more rapidly than the body weight.\textsuperscript{36-40} In any case, a radical shift takes place in the relative hemodynamic load ratio of the ventricles at the time when QRS--STT relationships change rapidly.

The progressively decreasing spatial angle between the QRS and STT integral vectors appears to be the main measurable determinant of the increase of the magnitude of the ventricular gradient vector from the third week of life until the age 1.5-4.5 years. At this age the concordance of QRS and T has reached its maximum level. This means that the general direction of repolarization at that age is, on the average, nearly opposite to the general direction of depolarization. At the cellular level this means that the fibers which are excited first should have the longest action potential durations, and the action potential duration would progressively decrease as some function of the excitation time.

We can only speculate what factors cause the likely increase in the magnitude of dispersion of action potential durations from third week of life to age 1.5 years. One explanation is the maturation of the sympathetic system and the development of sympathetic innervation of the cardiac musculature during this period. The sympathetic innervation developing first at the epicardial layers may progressively shorten the action potential durations at these layers. Consequently, those fibers which are excited latest would tend to repolarize first.

Again, we can only speculate how those relationships change later on in childhood, adolescence and adulthood when the QRS-T angle progressively increases again. With increasing left ventricular wall thickness, the QRS integral vector continues its shift to the left and posterior, while the STT integral vectors migrate clockwise more and more anteriorly. Possibly, the steadily increasing left ventricular wall thickness documented to take place throughout the childhood and adolescence\textsuperscript{44} changes the action potential duration profiles in the left ventricle, or the relative differences between the right and the left ventricle. However, the relative weight ratio of the right and the left ventricle is reported to remain constant in children after 2-3 months of age.\textsuperscript{42} This observation may again indicate that neural and other factors may well be as important as anatomic-hemodynamic parameters influencing QRS-T relationships.

The evolutionary changes in QRS and T patterns have important practical implications to clinical vectorcardiography and electrocardiography. Substantial changes take place in the normal ranges of diagnostic parameters, and some of these variations, such as that observed in the spatial angle between QRS and T vectors (fig. 7) during the first year of life, are quite drastic. Improved methods, such as computer analysis of pediatric ECG and VCG, may be required to achieve better discrimination between normal and abnormal records.

The confidence limits reported here for the Frank-lead variables of normal children are based on cross-sectional data. Guller et al.\textsuperscript{44} have shown in a group of 45 infants that the scatter of normal ranges based on cross-sectional data can be somewhat reduced if the measurements from the newborn period are available for prediction of normal values at 7-14 weeks of age. With increasing availability of longitudinal ECG data such prediction procedures may sharpen the discrimination between normal and abnormal ECGs in children.

Our data were derived from a homogeneous racial group of Caucasian Canadian children. There are likely to be significant racial differences in the QRS-T relationship, as was reported for the T-wave magnitude of Z lead during the first 72 hours of life by Guller et al.\textsuperscript{1} Finally, a modified Frank lead system was used in the present study. Riekkinen and Rautaharju\textsuperscript{44} have reported significant amplitude differences between records made at the fourth and the fifth intercostal space. However, the major observations and con-
conclusions of the present study would probably not be influenced by the choice of the horizontal level electrode positions.

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