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The ECG changes due to altitude and to catecholamines*

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Summary. In order to distinguish the effects of beta-receptor stimulation on the ECG from other factors during short-term adjustment to hypoxic aerohypoxia, the ECG of 19 volunteers were compared during moderately acute, stepwise exposure to high altitude (6,000 m) in a low pressure chamber, once with and once without beta-receptor blockade (propranolol), and after isoprenaline inhalation at ground level. The results show that beta-receptor stimulation accounts mainly for most ECG changes during altitude exposure, i.e., for the shortening of R-R interval, the lengthening of Q-T and in particular for the ST-T flattening, the latter therefore being only an indirect sign of hypoxia. After exclusion of the catecholamines, the minor but still significant ECG changes at altitude (shortening of R-R interval, increase of P wave, prolongation of P-Q, deviation of the R vector, T wave flattening in the left precordial leads) may be attributed to other, so far undefined factors, such as cardiac hypoxia, vagal withdrawal, or increase of pulmonary resistance.

Key words: Altitude – Aerohypoxia – Isoprenaline – Beta-receptor blockade – ECG changes

Introduction

The respiratory, circulatory, and ECG changes during standardized exposure to high altitude, described in a previous paper (Laciga and Koller 1976), were explained as being due to the vector sum of a number of influences of varying magnitude and direction. Except for hypoxic stimulus on the peripheral chemoreceptors, direct effects of oxygen deficiency are difficult to determine in healthy human subjects, mainly because of the great number of indirect effects. Among these indirect hypoxia-induced influences on the cardiovascular system, and in particular the ECG, are hypocapnia, i.e., respiratory alkalosis, and the activity of the sympatho-adrenal system, since it is well-known that the pituitary-adrenal axis is activated early in systemic hypoxia (Cunningham et al. 1965).

The role of catecholamines released during the short-term adjustment to hypoxia of the human organism was investigated in a further study (Boutellier and Koller 1981) with beta-adrenergic blockade (propranolol): Apart from the respiratory and circulatory reactions at altitude, the ECG changes during myocardial depolarization occurred in both the control and the propranolol groups, results pointing to possible direct effects of hypoxia on the myocardium. During the repolarization phase, however, beta-adrenergic blockade led to an almost complete abolition of the S-T depression and to significant reduction of the T-wave flattening. The minor but still significant flattening of the T wave, as well as the relative (to the heart rate) Q-T lengthening of the beta-receptor blocked subjects at altitude, was thought to be due to direct effects of hypoxia. The increase in ventilation at altitude, and thus respiratory alkalosis, were too small to underlie significant cardiovascular reactions and ECG changes.

The results found per exclusionem, i.e., blockade of beta-receptors, show that hypoxia-induced release of catecholamines contributes essentially to the ST-T flattening at altitude, and it might be suggested that the ECG at altitude equals the ECG due to catecholamines. The purpose of the present investigation was therefore to compare the hypoxia-induced ECG changes at altitude with those after isoprenaline

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* Dedicated to Prof. O. A. M. Wyss on the occasion of his 80th birthday

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inhalation (at ground level) in order to define positively the effect of beta-receptor stimulation, and to distinguish the latter from other hypoxia-induced influences. A preliminary abstract of this work has been presented (Saurenmann and Koller 1982).

It was reported recently by Swanström and Bratteby (1982) that our "subjects exposed to simulated altitude were not hypoxic" and that our results, described above, were "unspecifically positive and due to increased sympathetic tone and/or hyperventilation induced by the test situation in the low pressure chamber". In spite of this surmise, the experimental conditions were not changed and remained the same as in our previous papers. But it should be emphasized (once more) that the stepwise ascent was limited to 6,000 m as a precaution for the subjects, because exposure to an altitude above 6,000 m may result in inadequate respiratory and cardiovascular adjustments to hypoxia with imminent vagotonia and loss of consciousness, as already reported by Laciga and Koller (1978).

Methods

1. Subjects

The experiments were carried out on 19 healthy, male students with normal ECG at rest as well as during exercise. The work capacity of the participants corresponded to that of normally trained subjects (Bühlmann 1965). The informed consent of all volonteers was obtained.

2. Electrocardiography, pneumotachography, air mass spectrometry, low-pressure chamber

The techniques used have been fully described in a previous paper (Laciga and Koller 1976): Bipolar limb leads (Einthoven I, II, and III) and unipolar precordial leads (Wilson V_1-V_6) were recorded by a scalar ECG-unit input (EMT 83) of an eight channel ink-jet oscillograph (Mingograph 800). Blood pressure and pulse rate were automatically registered (ELAG, BE 207-S). Ventilation was recorded by a Fleisch pneumotachograph, the respiratory gases were continuously analyzed by a mass spectrometer (M3, Varian MAT). V_2, V_4, V_6 as well as PAO_2 and $PACO_2$ were monitored as a control of the test person. Altitude was simulated in a low-pressure chamber with the test subject at rest in a supine position.

3. Isoprenaline inhalation, beta-receptor blockade

Isoprenaline inhalation was standardized (three blasts of the isoprenaline aerosol Medihaler forte). This dose of isoprenaline – as found empirically – induced analogous electrocardiographic changes, in particular with regard to the ST-T depression, as in the ascent to 6,000 m in the low pressure chamber.

Beta-receptor blockade was achieved by propranolol (Inderal) given orally in three successive doses (80 mg, 40 mg, 40 mg) within 14-h prior to the start of the experiment. The validity of the beta-receptor blockade was tested by standardized isoprenaline inhalation; the latter was repeated after an interval of 5-min to prevent accidental non-responsiveness (see below).

4. Experimental procedure

Each test subject underwent two ascents in the low-pressure chamber, one without and one with beta-receptor blockade, the sequence being randomized. The interval between the two experiments was 1–2 weeks.

A few days before the first experimental session, the subjects were clinically examined (ECG, work capacity). "Moderately acute" ascent (Van Liere et al. 1963) from ground level (450 m) to 6,000 m – carried out at a rate of 1,000 m per 2-min – was interrupted for the first time at 2,000 m, then every 1,000 m by a 20-min pause, which permitted registration of the cardiovascular and respiratory parameters. The ensuing descent proceeded similarly in 1,000 m steps. The duration of the entire altitude exposure, including the adaptation time before ascent, was about 4 h. During this period, the test person was under the constant supervision of two physicians, one in the chamber, the other outside, monitoring the subjects by means of television, radio, and continuous ECG and ventilation displays.

After descent to ground level the isoprenaline spray was applied. In the propranolol group, isoprenaline-inhalation served as a test for the validity of the beta-receptor blockade (see above).

5. ECG evaluation

Although ECG was registered and evaluated every 1,000 m during both ascent and descent, in what follows, the results were restricted to the control at ground level and to the three test situations, i.e., at altitude, with or without propranolol, and with isoprenaline inhalation.

The records of the ECG (as well as those of ventilation and respiratory gas concentrations) were measured under a magnifying-glass scale with an accuracy of 0.1 mm.

Duration of the ECG segments. Regarding the time scale (5 $cm \cdot s^{-1}$), the accuracy of evaluation amounted to 0.01 s. Special attention was paid to the heart rate (R-R interval), P-Q interval, and Q-T duration. According to Holzmann (1961), the averaged value of the P-Q interval in Einthoven's leads I, II, and III was considered as the A-V conduction time.

Q-T duration of all leads was measured from the beginning of the Q wave to the intersection of the down-slope tangent of the T wave with the isoelectric line. The duration of electrical systole could not be taken in any lead from the first appearing Q wave to the last deflection of the T wave, because not all leads were registered synchronously. In consequence, again according to Holzmann (1961), the maximal Q-T was taken as the duration of electrical systole.

In addition to this absolute or "measured" Q-T value, the theoretical duration of the Q-T interval in relation to heart rate was calculated, using the formula of Hegglin and Holzmann (1937): "calculated" Q-T = $0.39 \cdot \sqrt{\overline{R\text{-}R}}$. The differences between measured and calculated Q-T, both given as mean values, were interpreted as "relative changes". Furthermore, the correlations between measured Q-T and R-R interval were determined by linear regresssion; the slope of the regression lines are comparable to the "corrected Q-T" of Puddu et al. (1982).

Voltage of the ECG segments. The amplitudes of P, Q, R, S, and T waves were measured using the P-Q segment as the zero line. The

evaluation accuracy amounted to 0.01 mV. As particularly the potentials of the QRS complex decrease as a function of inspiration, the amplitudes were averaged during a respiratory cycle.

Apart from the T-wave amplitude, the voltages of the subsegments ST_1-ST_5 were measured in four equal intervals of the entire ST-T segment.

In order to summarize the different leads, vector planogramms were constructed in the frontal—using the triangle of Einthoven – and in the transversal plane – using Wilson leads –. ST_4, corresponding more or less to the maximal amplitude, figures as "T vector", since the T-wave amplitude, not recorded at the same time in the different leads, was not available for this purpose. P, R (mean electrical axis) and T vector in the frontal plane are given by voltage and angle to the transversal axis, whereas in the transversal plane only the T vector is illustrated, because the intrinsic deflection (rS) or "proximity effect" of the ventral precordial electrodes (Hopff et al. 1963) masks changes of the R vector in this projection.

Statistical analysis. Mean values and standard deviations were calculated. Comparing the same subjects under different conditions, the statistical significance of the differences between the test situations and the control was determined by the paired *t*-test. Direct comparison of the ECG at altitude and after inhalation of isoprenaline was not carried out, since the dose of isoprenalin was chosen in order to induce an analogous ST-T flattening as during altitude exposure (see above). The following limits for two-tailed significance were established: $2P < 0.05$ *, $2P < 0.01$ **, $2P < 0.001$ ***.

Results

As pointed out in the methods, the evaluation was restricted to the electrocardiographic changes before (control) and during the three different test situations, i.e., exposure to altitude without (1) and with (2) beta-receptor blockade and (3) isoprenaline inhalation. Respiratory parameters are given so far as necessary for the interpretation of the ECG-changes.

All subjects tolerated the ascent to high altitude subjectively well and without major objective impairement. At 6,000 m the subjects felt tired, dozed or showed a certain weakness of attention and perception of which they themselves only became aware when the symptoms disappeared in the course of descent. In general, the second ascent appeared to be subjectively easier, particularly when combined with beta-receptor blockade. In contrast to exposure to altitude, the three blasts of isoprenaline were often experienced as unpleasant, because of the catecholamine-induced psychic tension and cardiac palpitations of the non-blocked subject. For the validity of the beta-receptor blockade see below.

Table 1. Respiratory and electrocardiographic parameters at ground level (Control), at high altitude without and with beta-receptor blockade (BRB) and after isoprenaline-inhalation

	Control (450 m)	Altitude (6,000 m)	Altitude + BRB (6,000 m)	Isoprenaline (450 m)
1. Respiratory parameters				
$\dot{V}_E$ ($l \cdot min^{-1}$)	7 ± 1	10 ± 3	10 ± 2	8 ± 1
PAO_2 (mm Hg)	95 ± 4	31 ± 3	31 ± 4	101 ± 6
$PACO_2$ (mm Hg)	38 ± 2	29 ± 2	29 ± 2	33 ± 3
2. ECG parameters				
a) Duration				
P-Q (s)	0.16 ± 0.02	0.16 ± 0.02	0.17 ± 0.02***	0.15 ± 0.02*
Measured Q-T (s)	0.37 ± 0.03	0.35 ± 0.03***	0.37 ± 0.02	0.38 ± 0.03
Calculated Q-T (s)	0.37 ± 0.03[a]	0.31 ± 0.03***[a]	0.35 ± 0.03**[a]	0.33 ± 0.04***[a]
b) Vectors in the frontal plane				
P vector direction (°)	65 ± 12	69 ± 6	66 ± 7	67 ± 7
potential (mV)	0.17 ± 0.05	0.21 ± 0.05***	0.18 ± 0.05	0.19 ± 0.06
R vector direction (°)	70 ± 13	67 ± 14**	70 ± 13	69 ± 14
potential (mV)	1.63 ± 0.58	1.45 ± 0.55***	1.50 ± 0.53*	1.47 ± 0.53***
T vector direction (°)	51 ± 19	30 ± 46*	47 ± 21**	45 ± 28
potential (mV)	0.38 ± 0.12	0.22 ± 0.11***	0.34 ± 0.12	0.24 ± 0.10***
c) T amplitude in different leads				
I (mV)	0.31 ± 0.09	0.19 ± 0.09***	0.28 ± 0.09	0.21 ± 0.07***
II	0.42 ± 0.14	0.22 ± 0.16***	0.38 ± 0.14*	0.24 ± 0.15***
III	0.16 ± 0.13	0.06 ± 0.14***	0.11 ± 0.14*	0.07 ± 0.15**
V_2 (mV)	0.70 ± 0.19	0.57 ± 0.23***	0.67 ± 0.25	0.55 ± 0.16***
V_4	0.78 ± 0.23	0.42 ± 0.28***	0.65 ± 0.20**	0.50 ± 0.20***
V_6	0.49 ± 0.24	0.23 ± 0.19***	0.43 ± 0.19	0.30 ± 0.11***

Values are means ± SD; $n = 19$

* Statistical significance of electrocardiographic differences between test situation and control: $2P < 0.05$

** $2P < 0.01$

*** $2P < 0.001$

[a] Statistical significance of difference between measured and calculated Q-T in the same test situation

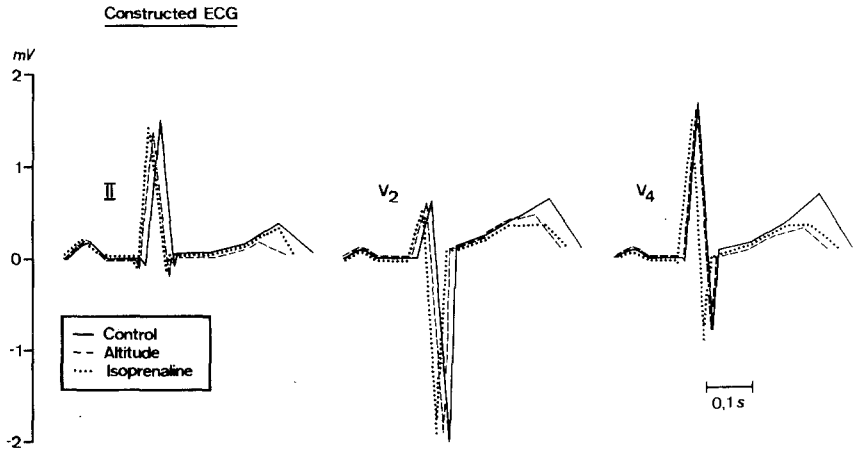

Fig. 1. Constructed ECG of limb lead II and precordial leads V_2 and V_4 under control conditions, during exposure to high altitude (6,000 m) and after isoprenaline inhalation. (Mean values; $n = 19$)

The changes in ventilation due to altitude exposure with and without propranolol, and after the ensuing isoprenaline administration are listed in Table 1. Propranolol on the one hand was obviously without effect on hypoxia-induced hyperventilation, venous pH thereby never exceeding 7.40. Isoprenaline on the other led only to small changes in ventilation which hardly contribute to electrocardiographic changes.

a) General electrocardiographic changes

The electrocardiographic changes occurring at altitude and after isoprenaline inhalation are shown in Fig. 1. Both test situations led partly to parallel, partly to opposite changes in the duration and voltage of the particular ECG segments. The most impressive alteration in both test situations was depression of the ST-T segment, which revealed, however, distinct differences in prevalence between altitude exposure and isoprenaline (see below). The T-wave flattening at altitude, although almost abolished, was still significant in some leads of the ECG after beta-receptor blockade.

b) Particular electrocardiographic changes

1. Changes in the duration of the ECG segments. In Table 1, the duration of P-Q as well as of Q-T are listed. Q-T is given in absolute terms ("measured" values). In addition, "calculated" values are listed in order to indicate the hypothetic Q-T duration with regard to the heart rate in question.

Although, on an empirical basis, both test situations, i.e., isoprenaline inhalation in the described dose and exposure to 6,000 m, affect the ST-T segment to a similar extent, the increase in heart rate related to the respective control value was more pronounced at altitude than after isoprenaline

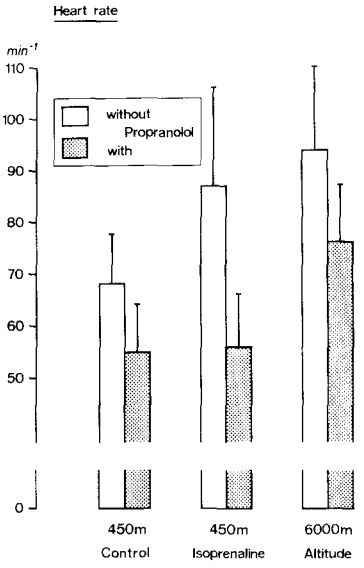

Fig. 2. Heart rate of subjects with and without beta-receptor blockade under control conditions, during exposure to high altitude (6,000 m) and after isoprenaline inhalation. (Values are means ± SD; $n = 19$)

(Fig. 2). Parallel to the control, an increase in heart rate due to altitude exposure was also found in the beta-receptor-blocked subjects who, of course, exhibited a lower heart rate and failed to show an effect after isoprenaline inhalation. This non-responsiveness to repeated isoprenaline inhalation served as a test of validity for the beta-receptor blockade (see methods).

A-V conduction time. Since the interindividual P-Q interval did not correlate with the corresponding heart rate, P-Q is given only in "absolute" values (Table 1). Isoprenaline reduced the P-Q interval significantly in contrast to altitude exposure, during which P–Q did not differ from the control, in spite of the markedly increased heart rate; in other words, in subjects exposed to altitude, the P-Q interval was

lengthened relative to heart rate. This P-Q prolongation was highly significant even in absolute terms after beta-receptor blockade.

Electrical ventricular systole. The duration of QRS in all three test situations was not significantly altered. The Q-T interval after isoprenaline was not significantly changed but relatively prolonged, if the increase in heart rate was considered (the measured value in Table 1 is significantly higher then the calculated term). Also at altitude, the Q-T was prolonged in relation to the increased heart rate, although the measured Q-T interval was unchanged with and even shortened without beta-receptor blockade. In Fig. 3, the measured Q-T interval of the different test situations is shown as a function of the heart rate. The shaded area represents the range of Q-T in relation to heart rate according to the formula of Hegglin and Holzmann (1937), which corresponds well with our control group. A strong correlation between heart rate and Q-T interval was found at altitude ($r = 0.77$) as well as under control conditions ($r = 0.87$), this being in contrast to the isoprenaline group ($r = 0.26$).

2. Changes in the voltage of the ECG segments. Some of the results are figured as vectors, either in the frontal plane, i.e., calculated from the standard limb leads, or in the transversal plane, determined, if possible (see methods), from the precordial leads.

The changes of the P, R, and T vector in the frontal projection are listed in Table 1.

Depolarisation of the atria. Although changes of the P wave are not visible in Fig. 1, the P amplitude in comparison with the control was significantly increased at altitude in bipolar lead II ($P < 0.001$) and in lead III ($P < 0.001$), resulting in a significant prolongation of the P vector and a slight rotation to the right (Table 1). Isoprenaline as well as altitude exposure in beta-receptor-blocked subjects failed to produce such clear alterations.

Depolarisation of the ventricles. Both altitude and isoprenaline reduced the R wave (Fig. 1). The reduction of the R vector at altitude is still significant after beta-receptor blockade. In contrast to these concordant effects, only altitude exposure without propranolol led to a significant deviation of the mean electrical axis due to the reduction in size of the angle of the latter (Table 1).

Repolarisation of the ventricles. The flattening of the ST-T segment, as already pointed out, was the most obvious electrocardiographic effect of altitude exposure and of isoprenaline inhalation. The S-T segment was never displaced below the isoelectric line. ST-T depression, however, was found in all leads, except in precordial lead V_1 where, on the contrary, the T wave

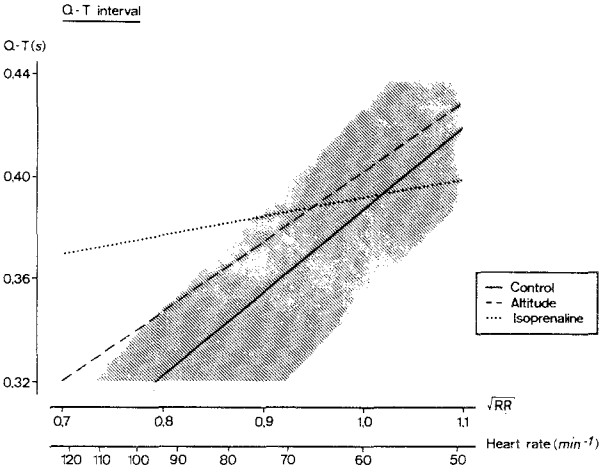

Fig. 3. Regression lines between Q-T interval and heart rate under control conditions, during exposure to high altitude (6,000 m) and after isoprenaline inhalation, compared with the variation range (hatched area) given by Hegglin and Holmann (1937). ($n = 19$; for mean values and SD of measured Q-T, Table 1)

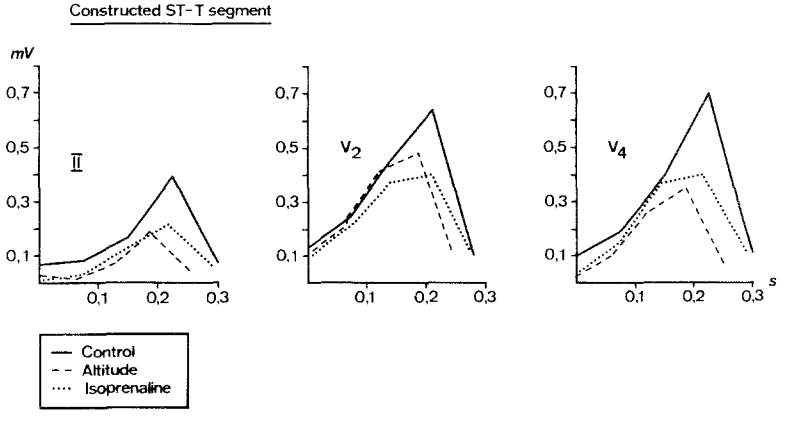

Fig. 4. Constructed ST-T segment of limb lead II and precordial leads V_2 and V_4 under control conditions, during exposure to high altitude (6,000 m) and after isoprenaline inhaltion. (Mean values; $n = 19$; for SD and significance of differences, Table 1)

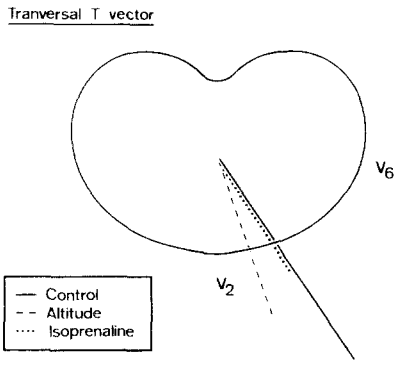

Fig. 5. Transversal projection of T vector determined from precordial leads (Wilson) under control conditions, during exposure to high altitude (6,000 m) and after isoprenaline inhalation. (Mean values; $n = 19$; for significance of differences, see text)

was significantly increased during altitude exposure ($P < 0.001$) and after isoprenaline ($P < 0.01$). In general, however, the amplitude of the T wave was reduced in both test situations (Table 1), but with different prevalence: Isoprenaline affected all leads equally, altitude exposure, however, showed a clear preponderance of T-wave flattening in the left precordial leads (Fig. 4). This difference is vectorially presented for the transversal plane in Fig. 5: At altitude the T vector exhibits a significant deviation ($P < 0.01$) to the right (70°), after isoprenaline and during exposure to altitude with beta-receptor blockade the angle in the transversal plane was 56°, i.e., similar to the control (55°).

The magnitude of the transversal T vector is, according to the previously described scalar terms, significantly reduced during exposure to altitude ($P < 0.001$) and after isoprenaline inhalation ($P < 0.001$). At altitude this reduction was not significant in subjects with beta-receptor blockade. Also, in the frontal plane (Table 1) the T vector is significantly shortened during exposure to altitude and after isoprenaline inhalation, but only systemic hypoxia induced a significant deviation to the horizontal line, which may not be interpreted as a rotation to the left, as usually done, because Fig. 5 proves a clear rotation to the right.

Discussion

The results presented show that many of the altitude-induced electrocardiographic changes can be simulated qualitatively by means of isoprenaline inhalation. These, in context with our former published findings, allow us to conclude that catecholamines mainly determine the ECG changes at altitude, the latter therefore being only indirect "signs of hypoxia" (Swanström and Bratteby 1982; Tuchschmid et al. 1981).

The dose of isoprenaline was determined empirically in order to induce a degree of ST-T flattening similar to that during exposure to 6,000 m, since depression of this segment is the most significant alteration of all electrocardiographic parameters: A quantitative comparison of the isoprenaline applied with the circulating beta-receptor mimetics at altitude – the latter in the mean-time have been determined (Koller et al. 1983) – appears to be problematic. But it should be pointed out that the increase in catecholamines during altitude exposure is relatively low, and mainly due to increased release of norepinephrine. The increase of circulating epinephrine was, besides the minor but significant hypoxic influence, mainly due to psychic tension.

Other factors – besides the catecholamines – affecting the ECG at altitude (cardiac hypoxia, vagal withdrawal, increase of pulmonary resistance) play a minor role (see below). Effects on the ECG arising from blood pH (respiratory alkalosis or hypoxic acidosis) have been excluded in our previous experiments (see Introduction).

Changes in the duration of the ECG segments

In spite of analogous ST-T changes at altitude and after isoprenaline inhalation, the heart rate differs significantly in the two situations. The higher heart rate at altitude may, in addition to the effect of catecholamines, be explained by vagal withdrawal due to systemic (or central) hypoxia, since a parallel increase in heart rate (although at lower level) is also found during altitude exposure in the subjects with beta-receptor blockade, the validity of the latter having been tested after each experiment. Competitive effects of endogeneously released catecholamines can be excluded.

The P-Q interval was clearly shortened after isoprenaline inhalation, but at altitude it was lengthened, particularly when the influence of catecholamines was excluded (altitude with propranolol). Surprisingly, altitude has no effect on the P-Q interval of subjects without propranolol, in spite of the markedly increased heart rate. This paradoxical "negative" effect may be due to two opposite influences arising from the catecholamines (positive dromotropic effect) on the one hand, and from hypoxia on the A-V conduction fibres (negative dromotropic effect) on the other. This conclusion agrees well with the findings of Senges et al. (1980) who showed – by examining the combined effects of hypoxia and orciprenaline on the electrical activity of the sino-

atrial (SA) and atrioventricular (AV) nodes – that "orciprenaline restores the reduced nodal function at moderate hypoxia, but markedly potentiates the depression of automaticity and conduction in SA and AV nodes at severe hypoxia".

As generally accepted (Hegglin and Holzmann 1937), the Q-T interval in the control group is highly dependent upon the heart rate. At altitude, a similar correlation was found, the mean Q-T being somewhat shorter, because of the increased heart rate. In contrast to the findings at altitude, however, the isoprenaline group is characterized by a (relatively and absolutely) prolonged Q-T interval. The isoprenaline-induced prolongation of the Q-T interval is astonishing and hard to explain, since "beta-adrenoceptor occupancy in cardiac cell membranes enhances calcium-dependent slow inward current" (Reuter 1981). On the other hand, Q-T formulae for calculating relative (or heart rate-dependent) Q-T changes are developed for physiological heart rate changes and not for those due to drug application. Apart from the relatively prolonged Q-T, the ECG changes at altitude obviously did not exhibit much of the betamimetic influence (see above). For this weak effect at altitude, the longer – compared with the isoprenaline tests – experimental duration may be responsible, as suggested by Biberman et al. (1971), who attributed the prolongation of the "corrected" Q-T interval to the "hysteresis effect" owing to catecholamines.

Changes in the voltage of the ECG segments

The increased P wave in bipolar leads II and III during exposure to altitude, as already described by Peñaloza et al. (1958) and Laciga and Koller (1976), might correspond to a P pulmonale. Although it can be prevented by propranolol application, the increased P wave is not due to catecholamines, as isoprenaline inhalation is without effect. Propranolol, by reducing the stroke volume and heart rate, possibly prevents right heart overloading during altitude exposure. To what extent pulmonary vascular resistance increased in our experiments was not determined.

The total potential of the QRS complex, especially the R wave in both the bipolar and unipolar leads, decreased after isoprenaline inhalation as well as during altitude exposure, but to a significantly smaller extent at altitude in beta-receptor blocked subjects. These findings lead to the conclusion that catecholamines account mainly for the R-wave reduction. For the effects of other factors involved at altitude, such as hyperventilation, mechanical alterations of the heart position, increase in girth of the chest etc., see Laciga and Koller (1976). According to these authors, the mean electrical axis shows a deflection of the horizontal line during altitude exposure, whereas it was unchanged in the other test situations, a fact which points to other factors than catecholamines; for the concordant deviation of the T vector, see below.

The flattening of the T wave is the most impressive electrocardiographic alteration at altitude, but also after isoprenaline. That the decrease in T-wave amplitude was about the same after isoprenaline and during altitude exposure, was due, as already mentioned, to methodical factors. Propranolol, according to Boutellier and Koller (1981), leads to an almost complete abolition of the altitude-induced ST-T depression and to a significant reduction of the T-wave flattening. Thus hypoxia-induced release of catecholamines accounts mainly for the clinically significant ST-T depression, the latter therefore representing only an indirect "sign of hypoxia" (Swanström 1982; Tuchschmid et al. 1981). The minor but still significant flattening of the T wave in beta-receptor blocked subjects at altitude points possibly to direct effects of hypoxia on the myocardium, since severe hyperventilation and thus severe respiratory alkalosis, another possible factor in ST-T flattening (Lepeschkin 1957; Swanström 1982; Thomsen 1967, can be excluded. In addition, Furberg and Tengblad (1966) have shown that T-wave flattening due to voluntary hyperventilation could be abolished by beta-receptor blockade; Bibermann et al. (1971) explained the T-wave abnormalities during both hyperventilation and isoproterenol infusion as being due to asynchronous shortening of repolarization. But there are other differences between altitude- and isoprenaline-induced depression of the T wave: Whereas isoprenaline affects all limb and precordial leads to a similar extent, altitude has a clear prevalence for T wave depression in the left precoridal leads (V_4-V_6), as demonstrated by the direction of the T vector in the frontal and transversal planes. T-wave flattening without change in vector angle is solely induced by catecholamines, but the deviation of the T vector at altitude is not reproduceable by isoprenaline and is therefore the result of factors other than catecholamines. Beta-receptor blockade, however, inhibited this altitude-induced rotation of the T vector to the right in the transversal plane and upwards in the frontal projection as well as that of the R vector (see above). These contradictory results might be explained, in accordance with the interpretation of the increased P wave, by prevention of right heart overloading at altitude in beta-receptor blocked subjects. This interpretation finally would also explain in part why beta-receptor blocked subjects not only show essentially reduced electro-

cardiographic alterations, but also essentially improved subjective and probably objective tolerance to high altitude, because the level of hypoxia-induced cardiovascular reactions is lowered and myocardial oxygen consumption reduced (Jorgensen et al. 1973; Kumada et al. 1980).

In conclusion: Catecholamines account mainly for the ECG changes during subacute exposure to altitude (shortening of R-R interval, lengthening of Q-T, flattening of the ST-T segment). The minor but still significant ECG changes at altitude after exclusion of the catecholamines (shortening of R-R interval, prolongation of P-Q, increase in P wave, deviation of the R vector, depression of the T wave in the left precordial leads) are due to several so far undefined hypoxia-induced factors (cardiac hypoxia, vagal withdrawal, increase of pulmonary resistance). Direct cardicac effects of hypoxia can only be supposed. A further study dealing with the effects of altitude during vagal and complete autonomic blockade is planned.

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