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Physicians should seek to enhance the quality rather than the quantity of human life. Physical activity programs can increase life satisfaction through an immediate increase of arousal and a long-term enhancement of self-esteem and body image. In the young child competition can cause excessive arousal, but long-term adverse effects are rare. In the adult a reduction of anxiety and stress and a general feeling of well-being reduce the frequency of minor medical complaints, generating important economic benefits. Physical activity programs also help to correct the reactive depression that accompanies conditions such as myocardial infarction. Interest in physical activity should be stimulated from the earliest years of primary school. The allocation of curricular time to physical education does not hamper academic achievement. Rather, through its impact on psychomotor learning, it enhances the total process of intellectual and psychomotor development.

**Le médecin devrait chercher à améliorer la qualité plutôt que la durée de la vie humaine. Les programmes d'activité physique peuvent augmenter le degré de satisfaction dans la vie par une stimulation immédiate et une amélioration à long terme du respect et de la perception de soi. Chez le jeune enfant la compétition peut causer une stimulation excessive, mais à long terme les**

**effets défavorables sont rares. Chez l'adulte une diminution de l'anxiété et du stress et un sentiment général de bien-être réduisent la fréquence des doléances concernant des affections bénignes, produisant de la sorte des avantages économiques importants. Les programmes d'exercice physique contribuent également à corriger la réaction dépressive qui accompagne les maladies telles que l'infarctus du myocarde. L'intérêt envers les activités physiques devrait être stimulé dès les premières années d'école primaire. A l'intérieur des programmes d'enseignement, le temps consacré à l'éducation physique ne nuit pas à la réussite scolaire. Bien plus, par son impact sur l'apprentissage psychomoteur, il améliore le processus de développement intellectuel et psychomoteur.**

Most physicians measure service to the ill by a lengthening of life. Certainly most exercise specialists approach their task from this perspective. They will point to the studies that suggest that vigorous physical activity is associated with a halving of mortality from cardiovascular disease,<sup>1,4</sup> although the practical importance of small differences in longevity between experimental and control populations and the inferences derived from studies of self-selected volunteers have been questioned.

However, concentrating on longevity ignores the more important issue of the quality of life. A patient who has suffered a myocardial infarction will not be excited at the prospect that vigorous exercise will allow him to live 50.7 rather than 50.3 months. Rather, he is likely to enjoy exercise for its immediate reward: it makes him "feel better".

This paper will review the proposition that prolonged, endurance-type physical activity of moderate intensity, as currently prescribed, makes a person feel better. Benefits from a well designed physical activity program include increase of arousal, improvement of self-esteem and body image, relief of anxiety, stress and reactive depression, and maximization of intellectual and psychomotor development, all of which contribute to a "healthy mind".

### Arousal

Arousal is closely related to wakefulness or vigilance and may be objectively assessed by the performance of certain tests, such as determining the frequency at which a flickering light appears to be a continuously illuminated light. Arousal differs substantially from one person to another, and within an individual it shows a circadian rhythm, reaching its lowest level between 3 and 4 am, even if the subject attempts to remain awake. The physiologic basis of arousal is an increase in the activity of reverberating neuronal circuits in the reticular formation of the brain stem.

Human physical and mental performance shows an inverted U-shaped relation to the degree of arousal. If neuronal activity is insufficient a person feels bored, tired and even depressed. In contrast, overarousal leads to anxiety, nervousness, sleeplessness and poor performance. Medical treatment should suggest changes in occupation and lifestyle that will keep the individual at the peak of the arousal curve<sup>5</sup> (i.e., in a "eustress" condition<sup>6,7</sup>). Tasks that demand too much or too

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little from an individual lead to excessive stress, with adverse psychologic and psychosomatic consequences.<sup>8-11</sup>

The optimum level of arousal varies with the personality of the individual. An extrovert requires much greater stimulation than an introvert in order to reach optimum performance.<sup>12,13</sup> A second variable is the difficulty of the task that must be undertaken relative to the ability of the individual. More arousal is needed for performance of an easy task than one that is more difficult. A demanding executive appointment is in itself arousing, and optimum performance is then reached with much less external stimulation than in simple production-line employment. A third factor is environment. Any form of external stimulation increases arousal, whether this be noisy music, a cold draught or brightly painted walls. The ambience needed for an executive office suite thus differs markedly from what is desirable around a conveyor belt.<sup>5,14</sup>

#### *Activity and arousal*

Physical activity has a strong and immediate effect on a person's level of arousal. Movement stimulates muscle and joint proprioceptors, and the central projection of this information through spinothalamic pathways increases activity within the reticular neuronal loops.<sup>15,16</sup> For example, a driver on a deserted highway at night in a well heated car is in an environment that is bland in relation to the difficulty of the task. The level of arousal drops and the driver may fall asleep. A more appropriate level of cerebral function can be restored by getting out of the car and taking a brisk walk.<sup>14</sup> On the other hand, an overworked person who is an obsessive exerciser may find it difficult to fall asleep after a long stint of late-night jogging has increased arousal.

Chemical factors may increase arousal during and following physical activity. The stimulant action of drugs such as the amphetamines is well recognized, and there is increasing evidence that some disorders of affect are due to disturbances of catecholamine metabolism.<sup>11,17,18</sup>

Vigorous physical activity leads to

a release of both norepinephrine and epinephrine,<sup>19</sup> partly in the active regions of the brain, but also at the sympathetic nerve endings, which secrete norepinephrine plus small amounts of epinephrine. The triggering stimuli for this are a fall of central blood pressure and radiation of impulses from the motor cortex. The adrenal medulla, a third source of catecholamines, releases epinephrine if the activity is perceived as stressful or if the blood glucose level drops below 50 to 70 mg/dl (2.8 to 3.9 mmol/l).<sup>16</sup>

Mechanisms for the breakdown of the natural catecholamines are very efficient, and plasma levels of norepinephrine and epinephrine do not increase unless the intensity of activity is greater than 70% of the maximum oxygen intake or if there is the pressure of intense competition, such as during a hockey game.<sup>20</sup> However, failure to detect an increase of catecholamine production with lesser levels of activity is partly a criticism of technique. Brain catecholamines are largely excreted as 3-methoxy-4-hydroxyphenyl glycol (MHPG), while catecholamines from peripheral sources are eliminated as a mixture of MHPG and vanillylmandelic acid (VMA). We have observed an increase of plasma levels and urinary output of both MHPG and VMA with sustained exercise at only 40% of the maximum oxygen intake. The MHPG:VMA ratio in the plasma decreases during exercise but rises during recovery. The findings are consistent with a peripheral rather than a central secretion of catecholamines, with more ready excretion of VMA than of MHPG.<sup>21</sup>

It is tempting to suggest that physical activity increases arousal much as if one had taken a "shot" of Dexedrine (dextroamphetamine sulfate). Internal secretion of chemicals may contribute to the "runner's high", but our data suggest that changes in levels of cerebral catecholamines are minimal during moderate exercise.

A third possible variable governing interactions between mood and movement is the setting of the hypothalamic activity centre. Electrical stimulation of this region of the brain can persuade animals to run to exhaustion and even death.<sup>22,23</sup> Hu-

mans also seem to engage in physical activity until the hypothalamic centre is in some way satiated. This hypothesis can be tested very simply by asking a small boy to sit for an hour on a chair in the front parlour of his grandmother's house. The nature of the input to the activity centre is still uncertain but probably includes impulses from the hypothalamic temperature and glucose receptors, and feedback loops from the limb proprioceptors. If the combined input to the activity centre is inadequate, activity is increased until the "setting" of this regulator is reached.

"Hyperactivity" is probably an overworked diagnosis. Nevertheless, it is easy to envisage a situation in which the normal control setting of the activity centre is inappropriately adjusted. In some cases the individual concerned "feels good" despite too small a level of habitual activity to control obesity, while in other instances the midbrain centres demand an excess of activity, to the discomfiture of parents and teachers alike. Such a hypothesis certainly gives a simple explanation for the paradox that a hyperactive child can be helped by a chemical increase of arousal (through the administration of caffeine or amphetamines).<sup>24</sup> It also raises the possibility that control of overeating by the use of sympathomimetic amines may reduce activity, thus hampering efforts to create a negative energy balance.

#### *Competition and overarousal of children*

While some arousal is advantageous to performance, child psychologists and educators have argued that the intense arousal and heavy praise associated with minor-league sports have a harmful effect on children. It has been suggested that the normal scale of values is distorted and that the participants are subjected to excessive stress.<sup>25</sup>

Skubic<sup>26</sup> reported that a third of the students involved in little-league baseball became too excited to eat normally following competition and that in some instances arousal delayed the onset of normal sleep. While batting, the players' heart rates were high (148 to 195 beats/min), but recovery was rapid, the postgame heart rates averaging only

101 beats/min. Blimkie and associates<sup>20</sup> observed that boys excreted more epinephrine and norepinephrine during a hockey game than during an equivalent bout of cycle ergometer exercise. This effect was more obvious for players aged 16 and 23 years than for those aged 11 and 12 years.

The long-term influence of competition is small, though. Rivard and colleagues<sup>27</sup> had teachers evaluate students' behaviour before and immediately after participation in a major province-wide hockey competition. Before competition 88% were placed in the upper half of the class, and 82% of the participants maintained this category when they returned to school. Favourable scores were reported for motivation, group integration, school attendance and obedience. Frustration scores were generally the same before and after a match, irrespective of the outcome. A major determinant of behaviour was the attitude of the coach. A victory created a sense of achievement, but a loss was only well accepted if the coach showed enough maturity to accept defeat.

### **Self-esteem and body image**

Adequate self-esteem is an important facet of mental health. Regular physical activity may have indirect effects on self-esteem by increasing an individual's ability to undertake physical or mental work. It also has a direct impact on body image, one major factor influencing self-esteem. A sense of self-worth in turn influences lifestyle and thus general health.

The exercise specialist commonly assesses body image in terms of responses to Likert scales, in which the subject is asked to rate "my body as I would like it to be" and "my body as it really is" relative to a series of adjectival pairs such as "strong-weak" and "beautiful-ugly". Discrepancies arise between the two ratings if the subject has a negative self-image.

#### *Body image of the young*

Participation in a sports or physical activity program usually enhances the self-image of the young. In part this reflects adulation of successful young athletes. Neverthe-

less, gains are also registered by children who initially had a poor self-image, provided that the program is geared to their abilities and they receive appropriate praise for success they achieve.<sup>28</sup>

#### *Body image of the elderly*

Regular daily physical activity can also improve the self-image of a middle-aged or elderly person. Heinzmann and Baggeley<sup>29</sup> found that an 18-month conditioning program gave employees of the National Aeronautics and Space Administration a more positive self-image, with associated increases in stamina and energy, feelings of positive health and a greater ability to cope with stress.

Responses of adults are partly influenced by the gap between the perceived and the desired body image and also by the acceptance of the need for training. Thus, McPherson and collaborators<sup>30</sup> observed larger gains of self-image in patients who had suffered a myocardial infarction than in healthy subjects when the two groups undertook 24 weeks of training. A colleague and I<sup>31</sup> found that average scores of body image changed little for 65-year-old men and women who exercised for 3 months. An improvement in body image was registered by subjects who showed a good training response; those with little improvement of aerobic power had a wider discrepancy between actual and ideal body images.

#### *Implications for programming*

Improvements in body image undoubtedly encourage compliance with an exercise program. However, overzealous admonishment of an unsuccessful exerciser by a well built physical instructor can have a negative effect. Good judgement is needed to provide an effective stimulus to conditioning without the use of excessive persuasion.<sup>32</sup>

#### *Body image and lifestyle*

It has been suggested that an adverse lifestyle is one expression of alienation in the labour force.<sup>33</sup> The positive changes of mood and self-image that accompany an appropriately graded exercise program may have a favourable effect upon attitude to work and general lifestyle.

When the Canadian Health Hazard Appraisal test was given to participants in an employee fitness program the program adherents fared significantly better than controls over a 10-month period of evaluation, adding almost 2 years to their predicted lifespan through the correction of adverse health habits.<sup>34</sup> Given a 20% rate of participation in an employee fitness program, a corresponding increase of "useful" working life in the participants would yield an economic dividend of at least \$150 per employee per year, averaged over a 40-year workspan.

### **Anxiety, perceived health, stress and depression**

Because vigorous physical activity makes most patients feel better it also tends to reduce manifest anxiety, stress and depression, thus lessening the frequency of minor medical complaints and industrial absenteeism<sup>35</sup> as well as reducing health care costs.<sup>36</sup>

#### *Anxiety*

The influence of activity programs upon anxiety is greatly influenced by the initial status of the individual. When well balanced middle-aged men participated in a regular training program there was no change in manifest anxiety scores,<sup>37</sup> but in a preretirement exercise class there was a modest long-term decline of anxiety scores.<sup>31</sup> In the latter group the changes of score were largest in subjects who attended the class regularly but exercised at only a low intensity. This suggests that the observed response may have been due to group support rather than a more specific influence of the physical activity.

McPherson and collaborators<sup>30</sup> found significant decreases of manifest anxiety over 24 weeks of conditioning but commented that the change was more marked in those who had recently suffered a myocardial infarction. Among this group the participation in light recreational activity was sufficient to reduce anxiety scores.

#### *Perceived health*

Cheraskin and Ringsdorf<sup>38</sup> noted lower Cornell Medical Inventory scores in old people who were taking

daily exercise. Likewise, Palmore<sup>39</sup> commented that poor health (defined as more than 2 weeks of bed rest, more than three visits to a doctor or a stay in hospital for any one episode of illness) was four times more frequent among old people who took little regular exercise. Unfortunately, it is difficult to distinguish cause and effect in such studies.

In a longitudinal experiment on a preretirement exercise class a colleague and I<sup>40</sup> found that overall changes of Cornell Medical Inventory scores were slight but that there was a significant decline in positive responses to the section on miscellaneous diseases; in addition, subjects who had adopted a high-frequency/high-intensity pattern of training showed a decrease in the frequency of complaints relating to anxiety.

### *Stress*

Several reports have suggested that joggers have low scores on somatic indices of anxiety (e.g., heart rate and muscle tension) and that one long-term benefit of regular vigorous physical activity is a relief of chronic overarousal.<sup>41-45</sup>

Raab and Krzywaneck<sup>46</sup> and Cox and associates<sup>43</sup> have also claimed that physically active subjects show a below-average response to sensory and emotional stimulation. Other possible mechanisms for the commonly reported relief of mental stress include an improved oxygen supply to the brain,<sup>47</sup> a sense of greater control over one's destiny,<sup>48</sup> a reduction of type A behaviour,<sup>44</sup> an improvement of sleep habits,<sup>49,50</sup> a "conditioning" of the stress-and-strain mechanism through the physical demands of exercise,<sup>51</sup> and cognitive perceptions of the instrumental value of physical activity.<sup>52,53</sup>

It has been argued that much of present-day stress reflects the total submission to corporate objectives demanded of the modern executive, but questions have arisen about how far vigorous physical activity can provide a controlled outlet for hostile, aggressive impulses.<sup>54-56</sup> Although participation in contact sports has sometimes been recommended for this purpose,<sup>57</sup> a more likely outcome is a sense of guilt, with an increase of anxiety.<sup>58</sup>

Watching violent sports also seems to increase rather than to decrease aggressive tendencies.<sup>59,60</sup>

### *Depression*

The elevation of mood associated with regular physical activity seems particularly helpful in countering the acute reactive depression associated with conditions such as myocardial infarction.<sup>61</sup> Application of the Minnesota Multiphasic Personality Inventory (MMPI) to patients between 12 and 15 months after they were recruited to a post-coronary rehabilitation program showed that almost all the patients exceeded the theoretical depression score of 50 and that about one third had very high scores (more than two standard deviations greater than normal).<sup>62</sup> This subgroup also showed high values for the neurotic triad of hysteria, hypochondriasis and psychasthenia.

Brozek and collaborators<sup>63</sup> argued that men who subsequently suffered a heart attack had high initial scores for hypochondriasis. On the other hand, Ostfeld and coworkers<sup>64</sup> found no abnormalities of the MMPI in patients who subsequently had a myocardial infarction. I do not believe that the depression of the post-coronary patient has an inherent, constitutional basis. More probable reasons for the depression include weakness resulting from the heart attack and subsequent bed rest, sexual problems, inadequate or inappropriate advice from the attending physician, interaction with an over-anxious wife, frequent hospital admission and the patient's lack of confidence and fear of sudden death. The arousal and improvement of body image associated with a regular exercise program bring welcome relief from all of these natural reactions. A 4-year longitudinal study of 44 patients with particularly high scores for depression showed a substantial improvement in response to progressive exercise.<sup>65</sup> This finding is worth noting since many authors have maintained that the MMPI measures personality traits rather than mood state. More recently Kavanagh and I, using the Profile of Mood States test, found that patients had abnormal scores immediately after infarction but that the scores improved as the patients un-

derwent rehabilitation (unpublished observations, 1982).

### **Intellectual and psychomotor development**

#### *Intellectual development*

We know the value of regular physical activity; however, it is by no means easy for a physician to motivate a middle-aged adult to adopt a more active lifestyle. The process of indoctrination should begin in primary school.<sup>28</sup> While physical educators have urged such action for many years, school boards are often reluctant to sacrifice the necessary curricular hours, arguing that such a plan could stunt the intellectual development of children. This objection was recently examined in a study in Trois Rivières, PQ. Entire classes of primary school students undertook 5 additional hours of physical activity each week under the direction of a physical education specialist. Immediately preceding and succeeding classes at the same schools served as controls, following the standard Quebec primary school program of one 40-minute period of physical activity per week under the supervision of the usual classroom teacher.<sup>66</sup> The enhanced activity program produced the expected gains of maximum oxygen intake, muscle strength and physical performance but had no effect on growth.

Although the time available for classroom study was necessarily curtailed 13% to 14% by the activity program, the students in grades two to six from the experimental classes had consistently higher marks than the students in the control classes. Marks for French-language instruction were improved in 13 group comparisons, worse in 6 and unchanged in 26. Mathematics marks were improved in four group comparisons and unchanged in eight. There were lesser benefits in natural science and in English-language instruction. The only unchanged score was the mark awarded for behaviour.<sup>67</sup> This finding is at variance with the study done in Saskatoon by Bailey.<sup>68</sup> There, increased concentration and less disruptive behaviour was reported for students who devoted a lot of their class time to physical activity.

It could be argued that the marks observed at Trois Rivières reflected teachers' attitudes, since 80% of the teaching staff were in favour of the activity program, and the remainder were neutral rather than hostile. However, the gains in French-language instruction and mathematics were confirmed by independent province-wide examinations held during grade six. Moreover, any "halo" effect was subconscious, since the teachers were unaware that the girls benefited more than the boys from the additional activity. Teachers also suggested, in agreement with Bailey,<sup>68</sup> that the activity program improved behaviour, whereas objective reports for the classes showed that it did not.

Certainly the results are sufficient to show that the usual objection (lack of curricular time) to enhanced physical educational programs is invalid and that greater physical activity may even enhance academic performance. The results cannot be explained simply by improvements of body image. Involvement of the entire class avoided the complication of extra status that would have resulted from participation in the physical activity program by some students from each class. Arousal of the students by the exercise period may have increased their vigilance in the remaining classes, while a shortening of the working day for the usual classroom teachers may have enabled them to face their duties with greater vigour and enthusiasm.

### Psychomotor development

French psychologists have long insisted on the close relationship between psychomotor and mental growth. In the Trois Rivières study several attributes of psychomotor development were accelerated by the enhanced physical activity. The students in the experimental program had a more realistic perception of their stature than the controls, the advantage being particularly obvious in the youngest children (for whom the gymnasium program stressed psychomotor learning). Accuracy in estimating arm span was better in the experimental group. Recognition of the vertical plane and finger recognition also developed earlier in the experimental group than in the

controls.<sup>69</sup> These changes could all help the early stages of academic learning. Acquisition of numerical skills, for example, depends on use of the fingers,<sup>70,71</sup> and the impact of psychomotor learning on other skills, such as writing, is even more apparent.

### Conclusions

Obviously the early Greeks were correct when they emphasized the concept of a healthy mind in a healthy body. Today we should remember that one of the most important ways in which medical scientists can serve patients is by appreciating the link between the body and the mind and by seeking to fully develop human potential in both areas.

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## Prescribing Information

# Lopresor® (metoprolol tartrate)

50 mg and 100 mg tablets  
200 mg slow-release tablets

### Therapeutic Classification

Antihypertensive and anti-anginal agent.

### Actions

Metoprolol tartrate is a beta-adrenergic-receptor-blocking agent with predominant blocking effect on beta<sub>1</sub> receptors.

### Indications

#### a) Mild and Moderate Hypertension:

Usually used in combination with other drugs, particularly a thiazide diuretic, however, may be tried alone as an initial agent in those patients whose treatment should be started with a beta-blocker rather than a diuretic. The combination of Lopresor with a diuretic or peripheral vasodilator has been found to be compatible and generally more effective than Lopresor alone. Incompatibility with other antihypertensive agents has not been found, experience is limited however. Not recommended for the emergency treatment of hypertensive crises.

#### b) Angina Pectoris

Lopresor is indicated in patients with angina pectoris due to ischemic heart disease.

### Contraindications

Sinus bradycardia, second and third degree A-V block, right ventricular failure secondary to pulmonary hypertension, congestive heart failure, cardiogenic shock, anesthesia with agents that produce myocardial depression, e.g. ether and chloroform.

### Warnings

a) **Cardiac Failure:** Special caution should be exercised when administering Lopresor to patients with a history of heart failure, since inhibition with beta-blockade always carries the potential hazard of further depressing myocardial contractility and precipitating cardiac failure. In patients without a history of cardiac failure, continued depression of the myocardium can lead to cardiac failure. At the first sign of impending cardiac failure, patients should be digitalised and/or given a diuretic and observed closely.

Lopresor does not abolish the inotropic action of digitalis on the heart muscle, however, the positive inotropic action of digitalis may be reduced by the negative inotropic effect of Lopresor when the two drugs are used concomitantly. The effects of beta-blockers and digitalis are additive in depressing A-V conduction. If cardiac failure continues, despite adequate digitalisation and diuretic therapy, discontinue Lopresor therapy.

b) **Abrupt Cessation of Therapy with Lopresor:** Warn patients against abrupt discontinuation. There have been reports of severe exacerbation of angina, and of myocardial infarction or ventricular arrhythmias in patients with angina following abrupt discontinuation of beta-blocker therapy. The last two complications may occur with or without preceding exacerbation of angina pectoris. When discontinuation of Lopresor is planned in patients with angina, dosage should be gradually reduced over a period of about two weeks and the patient carefully observed. The same frequency of administration should be maintained. In situations of greater urgency, Lopresor should be discontinued stepwise, under conditions of closer observation. If angina markedly worsens or acute coronary insufficiency develops, it is recommended that treatment with Lopresor be reinstated promptly, at least temporarily.

c) Various skin rashes and conjunctival xerosis have been reported. A severe syndrome (oculo-muco-cutaneous syndrome) whose signs include conjunctivitis sicca and psoriasisiform rashes, otitis, and sclerosing serratitis has occurred with the chronic use of one beta-adrenergic-blocking agent (pilocarpine) but has not been observed with Lopresor or any other such agent. Physicians should be alert to the possibility of such reactions and should discontinue treatment in the event that they occur.

d) Severe sinus bradycardia may occur, in such cases, dosage should be reduced.

e) Lopresor may mask the clinical signs of continuing hyperthyroidism or complications and give a false impression of improvement. Therefore, abrupt withdrawal of Lopresor may be followed by an exacerbation of the symptoms of hyperthyroidism including thyroid storm.

### Precautions

a) Careful monitoring of patients with diseases associated with bronchospasm is mandatory and a bronchodilator must be administered concomitantly.

b) Administer with caution to patients subject to spontaneous hypoglycemia or to diabetic patients (especially those with labile diabetes) who are receiving insulin or oral hypoglycemic agents. Beta-adrenergic blockers may mask the premonitory signs and symptoms of acute hypoglycemia.

c) Adjust dosage individually when used concomitantly with other anti-hypertensive agents.

d) Closely monitor patients also receiving catecholamine-depleting drugs, such as reserpine or guanethidine. Lopresor should not be combined with other beta-blockers.

e) Appropriate laboratory tests should be performed at regular intervals during long-term treatment.

f) Lopresor should not be given to patients receiving verapamil. In exceptional cases, when in the opinion of the physician concomitant use is considered essential, such use should be instituted gradually, in a hospital setting, under careful supervision.

g) In patients undergoing elective or emergency surgery: Lopresor should be withdrawn gradually following recommendation given under Abrupt Cessation of Therapy (see WARNINGS). Available evidence suggests that the clinical and pharmacological effects of beta-

blockade induced by Lopresor are no longer present 48 hours after cessation of therapy.

In emergency surgery, effects of Lopresor may be reversed, if necessary, by sufficient doses of such agonists as isoproterenol or levaterenol.

h) **Usage in pregnancy and nursing mothers:** Lopresor crosses the placental barrier and appears in breast milk. It should not be given to pregnant women as it has not been studied in human pregnancy. If use of the drug is deemed essential in nursing mothers, the patient should stop nursing.

i) **Usage in children:** There is no experience with Lopresor in the pediatric age groups.

### Adverse reactions

**Cardiovascular:** Congestive heart failure (see WARNINGS), secondary effects of decreased cardiac output which include: syncope, vertigo, lightheadedness and postural hypotension; severe bradycardia, lengthening of PR interval, second and third degree A-V block, sinus arrest, palpitations, chest pains, cold extremities, Raynaud's phenomenon, claudication, hot flushes.

**Central Nervous System:** headache, dizziness, insomnia, mental depression, lightheadedness, anxiety, tinnitus, weakness, sedation, vivid dreams, vertigo, paresthesia. **Gastrointestinal:** diarrhea, constipation, flatulence, heart-burn, nausea and vomiting, abdominal pain, dryness of mouth.

**Respiratory:** shortness of breath, wheezing, bronchospasm, status asthmaticus.

**Allergic/Dermatological** (see WARNINGS): exanthema, sweating, pruritus, psoriasisiform rash.

**EENT:** blurred vision and non-specific visual disturbances, itching eyes.

**Miscellaneous:** tiredness, weight gain, decrease in libido. **Clinical Laboratory:** The following laboratory parameters have been rarely elevated: transaminases, BUN, alkaline phosphatase and bilirubin. Thrombocytopenia and leucopenia have been reported rarely.

### Symptoms and Treatment of Overdosage

**Symptoms:** bradycardia, congestive heart failure, hypotension, bronchospasm, hypoglycemia.

**Treatment:** Discontinue Lopresor and observe patient closely. In addition, if required, the following therapeutic measures are suggested.

1. **Bradycardia, and hypotension:** Initially 1-2 mg of atropine sulfate should be given intravenously. If a satisfactory effect is not achieved, a pressor agent such as norepinephrine may be administered after preceding treatment with atropine.

2. **Heart Block: (second or third degree)** Isoproterenol or transvenous cardiac pacemaker.

3. **Congestive heart failure:** Conventional therapy.

4. **Bronchospasm:** Aminophylline or a beta<sub>2</sub>-agonist.

5. **Hypoglycemia:** Intravenous glucose.

Large doses of isoproterenol can be expected to reverse many of the effects of excessive doses of Lopresor. However, the complications of excess isoproterenol, e.g. hypotension and tachycardia, should not be overlooked.

### Dosage and Administration

a) **Hypertension:** Initial Dose: 50 mg b.i.d. If adequate response is not seen after one week, dosage should be increased to 100 mg b.i.d. In some cases the daily dosage may need to be increased by further 100 mg increments at intervals of not less than two weeks up to a maximum of 200 mg b.i.d., which should not be exceeded.

**Usual Maintenance Dose:** 150-300 mg daily. When combined with another antihypertensive agent which is already being administered, Lopresor should be added initially at a dose of 50 mg b.i.d. After 1 or 2 weeks the daily dosage may be increased if required, in increments of 100 mg, at intervals of not less than 2 weeks, until adequate blood pressure control is obtained.

b) **Angina pectoris:** Initial Dosage: 50 mg b.i.d. for the first week. If response is not adequate, the daily dosage should be increased by 100 mg for the next week. The need for further increases should be closely monitored at weekly intervals and the dosage increased in 100 mg increments to a maximum of 400 mg/day in 2 or 3 divided doses.

**Usual Maintenance Dosage:** 200 mg/day. Dosage Range: 100-400 mg per day in divided doses. A dose of 400 mg/day should not be exceeded.

c) **Slow-release Lopresor SR 200 mg:** Lopresor SR 200 mg is intended only for maintenance dosing in those patients requiring doses of 200 mg per day.

Treatment must always be initiated and individual titration of dosage carried out using the regular tablets. Patients with hypertension or angina pectoris on a maintenance regimen of one 100 mg tablet twice daily may be changed to one Lopresor SR 200 mg tablet taken in the morning.

Lopresor SR 200 mg tablets should be swallowed whole.

### Availability

#### Lopresor

Tablet: 50 mg: Film coated, light red, capsule-shaped tablet, embossed 51 and scored on one side and GEIGY on the other.

Tablet: 100 mg: Film coated, light blue, capsule-shaped tablet, embossed 71 and scored on one side and GEIGY on the other.

#### Lopresor SR

Slow-release Tablet: 200 mg: Film-coated, light yellow, round tablet, embossed GEIGY on one side and CDC on the other.

Product monograph supplied on request.

### PAAB

### CCPP

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# Geigy

Mississauga, Ontario  
LSN 2W5

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