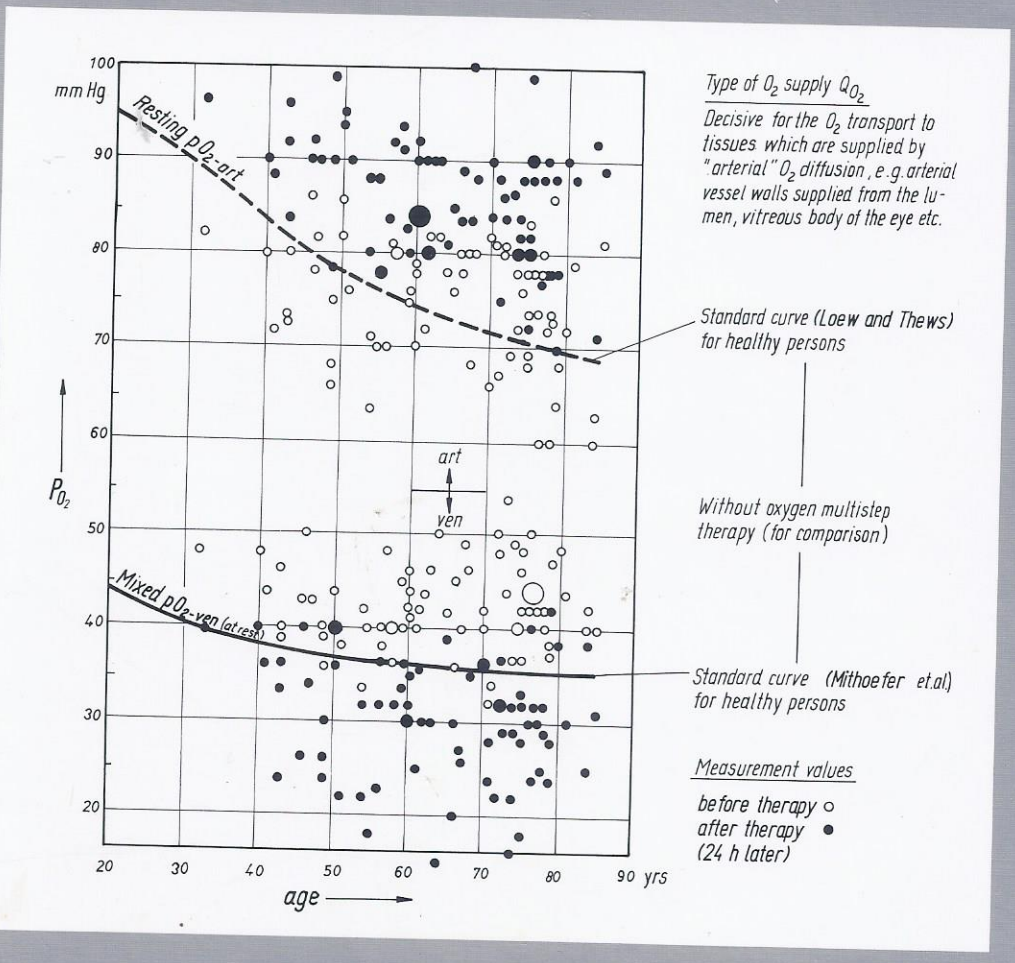
Oxygen Multistep Therapy

Physiological and Technical Foundations

Manfred von Ardenne



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Preface

In the late 60s, during our research into hyperthermic tumor treatment by whole-body heating, we were confronted with the problem of supporting the patient's cardiovascular and cardiopulmonal system by additional measures. The simplest and most natural way to do so was the application of oxygen, supplemented and accompanied by other supporting "steps". From the beneficial effects of this combination treatment we soon recognized that this regimen represents more than an adjuvant measure. Separate systemic studies during the past two decades resulted in the Oxygen Multistep Therapy (O_2MT) of today, which is now practised in some hundred medical centers, clinics, health spas and doctors' consulting rooms in about 12 European countries.

Starting from the common knowledge that, usually with increasing age, cellular energy production is much more limited by oxygen delivery than by nutrient supply, we have tried to improve the metabolic situation of weakened individuals by offering excess oxygen far below toxic concentrations (and amounts), combined with drugs that facilitate the intracellular oxygen turnover, and supplemented with physical exercise adapted to the individual performance level. This empirically found basic schedule has now developed and diversified into more than 20 different treatment variants. In contrast to the ad hoc use of oxygen in anesthesia, intensive care and emergency treatment, O_2MT as an ever repeatable modality aims at the permanent (or long-lasting) rehabilitation of the aging, weakened, stressed or otherwise afflicted patient by restoring an oxygen supply that is typical for younger healthy individuals.

To characterize a metabolically sufficient oxygen supply, there are well defined parameters: the arterial and venous oxygen partial pressures measured at rest and the oxygen saturation difference, η, derived from these. It will be shown in the book how innumerable measurements of these parameters, combined with others such as CO_2 production, cardiac output and ergometric data, led to the formulation of four discoveries, which form the backbone of O_2MT:

1. The discovery of a switching mechanism of blood microcirculation, which is effective in the whole body and controls, and depends on the oxygen supply and the capillary bloodflow;
2. The discovery that the oxygen-dependent "high-charging" of microcirculation results in effects lasting for months in terms of an improved energetic status;
3. The discovery that stressful events of the most varied kinds may severely compromise the oxygen ($\triangleq$ energy) status; this is, conversely, the explanation for the surprisingly broad field of applications of O_2MT;
4. The discovery of the close correlation between the quality of the oxygen ($\triangleq$ energy) status of an individual and the efficacy of the natural immune defense.

The largest part of the book deals with the treatment variants of the O_2MT and their indications. There are more than 20 direct or indirect targets of O_2MT in the body, the responses of which are the measurable proof for the beneficial effect of the treatment. The reader will find a broad spectrum of diseases which are in some way related to oxygen ($\triangleq$ energy) deficiency. It comprises circulatory disorders, myocardial infarction and mental disorders or complaints, and reaches up to problems of cancer immunology. However, it must clearly be stated that O_2MT is not able to cure severe acute or chronic diseases, although it can relieve side-effects of the established therapy regimens or attenuate the sequelae of the primary disease. By this, O_2MT decisively contributes to the improvement of the patient's general condition and considerably accelerates the phase of recovery.

Almost of the same importance in this context is the large field of everyday maladies, disorders and states of discomfort or lacking robustness, the grey zone between health and illness. This obviously poorly defined and sometimes neglected area is of utmost significance with respect to individual well-being and public health care and represents the other main target of O_2MT.

In order to establish Oxygen Multistep Therapy as it exists today, it was necessary to work out its technical basis. This included studies of the production or delivery of oxygen for clinical purposes at different scales and under different local conditions, as well as the effective, convenient and safe application of O_2 to the patient. This important complex is dealt with in a separate chapter.

This book, which is based on its 4th German edition (1987), applies to representatives of medical research as well as to practising physicians and also, to some extent, to the medically interested patient. All applications to date of O_2MT must be seen as pilot treatments in a wider sense. We hope that the ideas and results presented here will be tested critically, confirmed and extended by open-minded and unbiased physicians.

Dresden-Weisser Hirsch, Summer 1990

Manfred von Ardenne

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Introduction

The *amount of energy provision in the organism*, that is, primarily the resynthesis of adenosine triphosphate (ATP) according to the needs of the body, is the major factor influencing the health peaks and throughs of human life. This simple biophysical thesis is recognizable as a basic law of our existence when one remembers that the reduction in physical and mental powers, that is, energy deficiency, is a *main characteristic of extreme old age*. Furthermore, in this connection we should remember the *main characteristic of conditions of weakness of all kinds*, which is that in such phases the organism minimizes its energy requirements by lack of movement (e.g. bedrest), in order to ensure the balance between the critically reduced energy provision, and energy consumption. Finally, everyone knows that a high provision of energy is a *main characteristic of youth*. These considerations lead to a way of thinking that is still unusual in present day medicine, a way which may even at first seem disconcerting. But they force us to the conclusion that all events, mechanisms and processes which weaken, strengthen or even lastingly increase the provision of energy in the organism are of fundamental significance for both theoretical and practical medicine in particular for the prevention, prophylaxis and therapy of all diseases, crises or complaints with energy deficiency as their common cause. It follows that the *quantitative determination of energy provision in the human organism* leads to a comprehensive diagnostic characteristic value of exceptional significance.

Even after just the first steps along the way outlined the question of the *bottleneck in energy formation in the organism* appears. It is known that energy is generated in the organism mainly as chemical energy in the form of energy-rich phosphates, particularly as adenosine triphosphate (ATP) [1], discovered in Berlin-Dahlem in 1930 by K.H. Lohmann. Under normal living conditions the *formation of these energy-rich phosphates* is not limited by the intake of food but *by the oxygen transport to the body tissue*. The determination, the natural dynamics, and the process of increase in the O_2 transport to the body tissue become the key to further progress. We recognize that "Oxygen is the giver of life!" The words of Otto Warburg, which were repeatedly spoken in discussions with him in his Dahlem Institute of Cell Physiology, made a deep impression on the author. This, not only because they came from the researcher who contributed more than any other to the explanation of the respiration and fermentation metabolism of living cells, but because such a comprehensive biological basic truth is contained in this short theorem.

O_2 presents itself as the energetic prerequisite for the differentiation of cells in the slow phylogenetic and the fast ontogenetic development of more highly organized life. O_2 thereby also proves itself to be the prerequisite for the maintenance of life, and its deficiency leads to complaints, suffering, diseases or death.

The generic term "*O_2 deficiency*" can be defined as the combined or individual effect of *critically reduced O_2 transport* to the tissues (O_2 offer to the tissues), *critically reduced O_2 utilization* of the tissue, and *critically increased O_2 requirements* of the tissue.

The long-lasting (e.g. for weeks to months) amelioration or elimination of O_2 deficiency and, moreover, *an increase as strong and as long-lasting as possible in the O_2 transport to the body tissue, is the aim and effect of oxygen multistep therapy* (O_2MT).

Various procedure variants, some with different fields of indication, are practised. Alongside the 36 h O_2 multistep procedure, which requires more time and energy, a *15 min O_2 multistep quick procedure with simultaneous physical exertion* has been developed, which can free the organism from its deficient situation in just over 30 min. O_2 multistep short procedures have also been designed for nonable-bodied patients. For these patients the increase in cardiac output and in the respiration minute volume is brought about, not by physical exertion, but by drugs. All these procedures generally cause an increase in the arterial resting P_{O_2} and a drop in the mixed venous resting P_{O_2}, or an increase in the O_2 absorption and/or CO_2 production at rest, in addition to an increase in the physical performance capacity. Moreover, the improvement which occurs in the O_2 status is reflected in a shortening of reaction times and a drop in the "biological age", an improvement in infor-

mation-psychological capacity and an increase in the host's defense.

All O_2MT variants have in common the fact that, through the combination of several synergistic steps, the threshold of energy formation is crossed locally in the area of the capillary wall cells, by which the discovered cellular *capillary wall switching mechanism of the microcirculation* is switched in a positive direction.

In all variants of the "*oxygen multistep therapy*" [2, 3], the method of triggering the switching, i.e. to obtain the long-lasting effect, consists in the combination of the following basic steps:

1st step: *Increase in O_2 utilization* in tissues and cells by means of drugs taken approximately 30 min before start of step 2, e.g. 30 mg vitamin B_1, 75 mg dipyridamol, 100 mg magnesium orotate [4], possibly in the form of the combination preparation "Oxygenabund". For long-term effect the dose is continued once daily for an unlimited time.

2nd step: *Great increase in the O_2 partial pressure in the alveolar space of the lung* during the procedure, by supply of O_2, e.g. using applicators of synthetic material with storage balloon for a long [5] as well as for short duration of procedure [6], with a very high O_2 flow required. When the procedure duration is long, the O_2 flow should be arranged so that the alveolar P_{O_2} is increased from resting normal 100 mmHg (13.3 kPa) to approximately 200 mmHg (26.6 kPa), or so that the arterial P_{O_2} reaches levels close to 125 mmHg (16.7 kPa). For short procedure duration (< 1 h) oxygen-air mixtures are given at 60 to approximately 95 vol.-% O_2 using an applicator mask and adapting the O_2/N_2 flow to the patient's respiration minute volume (RMV) [6], which has been greatly increased by exertion.

In special cases (e.g. chronic lung damage, circulatory insufficiency, preshock conditions, emergency situations etc.), when the arterial pO_2 remains too low despite O_2 inhalation, additional immediate aid can be given by means of a simultaneously implemented HOT* procedure [7] (or i.v. administration of drugs to increase cardiac output), whereby the O_2 transport to the organism is substantially improved.

3rd step: *Increase in blood flow*, or at least the securing of good circulation in central organs such as heart and lung, or perhaps also of special areas of the organism [8] during the effect time of the 1st and 2nd steps [6]. Increase in cardiac output by physical exertion adapted to the patient's condition [6], or by drugs in nonable-bodied patients. Simultaneous occurrence of the 3rd step with the effect time of the other steps causes intensification, i.e. allows a significant reduction in time and oxygen [6] in the programming of the procedure. In the implementation as part of a cure (36 h O_2 multistep procedure) the physical exertion between the procedure session is planned as daily exercise training [9, 10, 11, 12]. In order to ensure a lasting O_2MT effect the daily exercise training is to be continued daily for an unlimited time. Use of the lastingly increased energetic status for an energetic lifestyle.

The *definition of oxygen multistep therapy* can be considered to be: O_2MT is a repeatable combination of measures for humans, carried out within a defined time-planned sequence, with the aim of a long-lasting increase in the resting O_2 uptake or in the arterial resting P_{O_2} and (or) reduction in the venous resting P_{O_2}. The practical result is an increase in the O_2 transport to the body tissue lasting for weeks to months, with a corresponding rise in the energetic status.

Each of the three steps has an individual, measurable effect and has been part of standard medical practice for a long time. As early as 1798 (!) a book reports on the use of oxygen as a cure [13]. But only when the three steps are connected as given, according to type and time-programming, does the rather surprising, lasting effect occur, i.e., as we know today, the *bioenergetic altering of the course of the discovered cellular vessel wall switching mechanism of the blood microcirculation in a positive direction and in all tissues of the organism*. This effect was hardly likely to be found under clinical conditions (e.g. in intensive care wards) as these, instead of increasing circulation as demanded by the 3rd therapy step, usually strongly reduce it.

In the last few years the time has become ripe for a broader preventative, prophylactic and therapeutic use of O_2 multistep principle. There are several reasons for this:

1. *The exercise-deficient lifestyle* (circulation deficit, drop in arterial P_{O_2}, O_2 deficiency) of people in industrialized countries has increased to a dangerous extent, and is still increasing. Motors have taken over physical labor. Microprocessors of modern electronics and robots increasingly control instruments, installations, machines and production processes of all kinds, without human involvement. Desk work, meetings, time spent travelling or in front of the television occupy an increasing proportion of our daily lives, both at work and in our free time.

2. Thanks to great medical progress in the combat of life-threatening diseases and conditions, *human life expectancy has greatly increased*, and more and more people reach old age, in which cardiopulmonal performance, and, with it, the O_2 supply to the tissues, drop to 50 % or less of the levels of youth. It is one of the current tasks of modern medicine to help these people by maintaining their physical and mental performance capacity and to make their lives worth living by the amelioration of the sufferings and complaints of old age.

3. It was not until the last decade that *instruments* were developed in the GDR (in our Institute), and more recently also in the FRG and the USA, which are operated from the electrical network, are easily transportable, and which, *by means of simple processes* (e.g. with zeolites or O_2 selective membrane systems) *enrich the oxygen from the atmospheric air* from approximately 20 % to 90 %. These new instruments facilitate the provision of inhalation air with an increased O_2 content, independent of heavy pressure cylinders as O_2 stores, and independent of central large installations (e.g. with liquid oxygen). This new type of instrument can make possible in the forseeable future the provision of O_2 even for households and areas of world health care in which the continuous provision of O_2 has so far caused difficulties.

4. Our discovery that the strength of the host's defense capacity is dependent on the quality of the O_2 status, and is significantly increased by the procedure of oxygen multistep immunostimulation, has opened the way to *bringing the length of one's own life close to the upper age limit of the human organism*.

5. Clinical 5-year results with oxygen multistep immunostimulation have shown that a significant *drop in the probability of metastasis in cancer* can be achieved with the course on which we have embarked, and that when the procedure is repeated once a year, even the concrete, simple solution of a *general* cancer prophylaxis emerges.

The primary target area of O_2 multistep therapy is the lung-heart system. In our investigations into this complex system we have found strong dynamics and reactivity in the co-acting parameters, which are reflected globally in changes in the arterial resting P_{O_2} (as a resultant). The occurring increase in the alveolar O_2 pressure (increase in the P_{O_2} of the lung ventilation by means of physical exertion) has a direct, therapeutic effect, particularly on the highly reactive alveolocapillary ventilation, perfusion and diffusion system of the lung. How exciting, then, from this point of view, was the first post-therapy finding of an increase in the arterial resting P_{O_2} to levels of nearly 100 mmHg or 13.3 kPa (!), lasting approximately 18 months, due to O_2 multistep therapy in a 70-year-old volunteer whose levels 6 years earlier were about 75 mmHg, or 10 kPa.

Particularly strong effects can be expected from the increase in the critically reduced arterial resting P_{O_2} caused by old age or stressful influences, and from maintaining this characteristic value at a permanently high level (repetition of therapy as stipulated by control measurements), when the pressure gradient for O_2 diffusion to the target area is determined *directly* by the arterial P_{O_2}. That is the case, for example, in the O_2 supply to the eye lens, to the cartilage, the vocal chords and the arterial vessel walls, when physiosclerosis generally leads to noticeable impairment after roughly the 50th year of life. The O_2 metabolism in the walls of the arterial vessels and of their highly-stressed branching points is fed to a large extent directly by O_2 diffusion from the lumen. The great increase in the arterial O_2 partial pressure which occurs *during* therapy, and the drop which usually occurs *after* our therapy, therefore have full effect in these crucial areas. Numerous findings on 50- to 70-year-old hypo- and hypertensive subjects with post-therapy blood pressure levels of around 135/75 mmHg or 18/10 kPa (≙ average levels of 30-year-old volunteers) give an idea of the renormalization of the RR levels (blood pressure measurement according to Riva-Rocci) or of the peripheral vascular resistance attainable through O_2 multistep therapy.

From the view of pathophysiology the new pos-

sibility of increasing more or less permanently the arterial P_{O_2} in older (and often also in sick) people, and of simultaneously reducing the venous P_{O_2}, means the opening up of a *natural causal prophylaxis and therapy for the many O_2 deficiency diseases and complaints of old age*. It is, after all, a return of the O_2 supply situation as in the best years of youth! In the foreground we can recognize a therapy measure that is permanently effective against arteriosclerosis, and a natural prophylaxis against myocardiac infarction – against the main causes of death in our time. A concrete methodology, close to nature, and of great universality is here ready for future preventative medicine.

Various influences and events have temporarily delayed the scientific recognition and assessment of the results of our O_2 multistep therapy research:

1. The long-term duration of an increase in the arteriovenous O_2 saturation difference *contradicted the experience and theories of the* pulmologists. But is it not precisely the unexpected, the surprising, that is the hallmark of a discovery?
2. As a result of methodological deficiencies which could easily have been avoided by prior consultation with us, the "switching threshold" of the discovered capillary switching mechanism of the blood microcirculation was not crossed in two important institutes and as a result our $P_{O_{2\text{-art}}}$ measurement results were not at first confirmed. These findings were unfortunately used as the basis of a series of discriminatory publications and hampering, premature decisions. In one of these institutes our findings on the lasting increase in the arterial P_{O_2} in volunteers with low starting levels were confirmed in autumn 1982. Our findings concerning the lasting drop in the venous resting P_{O_2} have not yet been considered.
3. Publication of our results in respected medical journals was repeatedly prevented by conservative, subjectively-judging members of the editorial boards. Such censoring touches a phenomen discussed worldwide in the pushing through of new scientific knowledge [14].
4. Since the author changed in 1960 from physics to medicine (since then 52 semesters of research study into medicine and physiology), O_2 multistep therapy was downgraded in some quarters as an "outsider method" [15, 16]. It was thereby overlooked that the medical research in our Institute has for many years rested on the basis of an integrated team of doctors, with internists and representatives of the branches of oncology, sports medicine, biology, biochemistry and biomedical engineering, and that a multidisciplinary view often brings with it many advantages.

The *basic effect of O_2 multistep procedures* (short definition η^+-effect), the long lasting increase in the resting O_2 uptake, or of the arteriovenous O_2 saturation difference of the blood, can no longer be seriously doubted. The *basic effect has been statistically proved with a large number of patients* (11 different studies with 2682 volunteers [17]) *and high significance*. Today it is reproduced daily in a good 300 cure institutions and in the process mainly rendered objective by O_2 measurements. Many tens of thousands of patients and volunteers have sensed in themselves the *increase in physical performance brought about by the basic effect*, which we could confirm directly *by ergometric measurements [6]. Most recently*, the lasting large increase in the O_2 metabolism in the organism after O_2MT could be directly proven by recording the CO_2 production of the lung (see Appendix).

An accumulation of reports of *good and very good treatment results* [18] can be noted for the indications: renormalization of the O_2 loading of the blood in the lung functionally degenerated by old age or severe stress; early stage of cataract, glaucoma, loss of field of vision, impaired focus; angina pectoris, arrhythmia, prophylaxis and rehabilitation for heart diseases; oedema; peripheral circulation disorders, especially in the lower extremities; circulation disorders, dizziness in old age, senile diabetes; hypotonia, Mb. Ménière; adjuvant therapy in hypertension, general acceleration of rehabilitation; lasting increase in physical performance capacity; defense stimulation, especially after classical cancer treatments, improved quality of life, e.g. in cancer patients.

Individual reports of interesting results, which challenge us to further inquiry, have been received for the following indications: memory weakness, conditions of confusion, side-effects of drugs taken over a long period of time, Parkinson's disease, multiple sclerosis, amelioration of migraine; amelioration of damage to liver and kidneys, amelioration of asthma; rheumatic symptoms complex; acceleration of wound healing.

On the basic of the hitherto amazingly good results, O_2 multistep therapy should prove to be exceptionally effective in the intensification of the host's defense system, and especially in

the implementation of a prophylaxis against cancer metastasis and even of a general cancer prophylaxis [19]. *The combination of the currently usual cancer therapy* (operation, chemotherapy, radiation therapy) *with an adjuvant triple procedure of O_2 multistep immunostimulation*, discussed in the last section of the book, can be immediately used in the fight against cancer, even in its later stages. The attractive feature of this concept, which is already clinically successful, is that the patient has all the advantages and effects which classical, normal cancer therapy can offer him in his case. But in addition, he gains amelioration of the side-effects of radiation and chemotherapy as well as, most importantly, often, or with a good probability, the prospect of a halt in the progression of his disease. A broad field for research into such central medical topics, which are decisive for medical practice, presents itself here. When all is said and done it is the improvement in the energy status that is the common key to the medical uses, which have certainly not been fully listed, of the basic effect of oxygen multistep therapy.

1. Physiological foundations

Energy is key
a.T.P.

1.1 Basic mechanisms and functions

1.1.1 The discovered cellular capillary wall switching mechanism of the blood microcirculation with varying effects in the lung and other body tissue

1.1.1.1 Ideas on the triggering of the switching mechanism of the blood microcirculation at the venous end of the capillaries

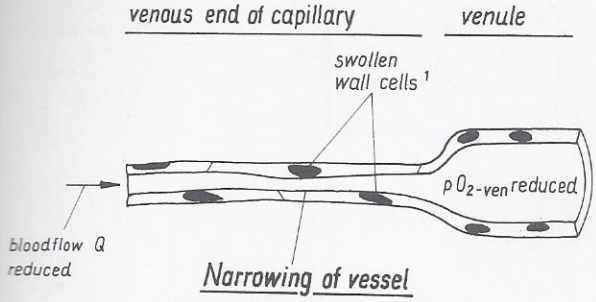
The basic effect of oxygen multistep therapy, the long-lasting increase in the arteriovenous O_2 saturation difference of the blood (η^+-effect), can, as suggested by numerous signs discussed below, be traced back to *a cellular vessel wall switching mechanism of the blood microcirculation*, which can be triggered by O_2 multistep procedures, and which chiefly starts from the endothelial cells of the capillaries. This switching, or regulating, mechanism is controlled bioenergetically, i.e. *by the energetic status* (hyperoxia and hypoxia) *of the endothelial cells or pericytes of the capillaries, and occurs in all capillaries of the organism simultaneously and concurrently*. It therefore has the fundamental characteristic of a comprehensive effect.

This mechanism is generally (but not always) reversible, i.e. the blood microcirculation can be strengthened by the switching effect (positive switching, η^+-effect) or weakened by it (negative switching, η^--effect). We were led to the discovery of this mechanism by the observations already mentioned that it generally *occurs in all capillaries of the human organism*. Its *effect is different in the lung and in other body tissue*. In the lung the bioenergetic control of the microcirculation leads to changes in the levels of the arterial pO_2, and in the other body tissues to changes in the venous pO_2. This mechanism is being discussed at the beginning of this book due to its fundamental significance for oxygen multistep therapy and the research connected to it.

The author obtained, in 1977, the first experimental clue that a reversible switching mechanism of the microcirculation (in the lung) must exist, from the surprising finding that the arterial resting pO_2, which falls greatly in old age, can by means of an O_2 multistep procedure of a total duration of approximately 36 hours, be raised to levels otherwise generally measured in youth [3]. Further clues resulted from the course of the arterial pO_2 levels measured after severe distress and subsequent combat of the consequences of stress [20]. The decisive clues presented themselves early in 1982 when it was discovered that O_2 multistep procedures also cause a lasting drop in the venous resting pO_2 [6]. In the course of this work, in interaction between literature studies and our own research into the selective staunching of the blood microcirculation in cancer tissues using the cancer multistep therapy measures [22, 23], increasingly concrete *ideas of the cell physiology of the bioenergetic control of the reversible switching mechanism of the microcirculation* were developed.

Stimulated by the intravital microscopic observations of Lübbers and co-workers on the electric triggering of changes in the cross-sections of capillaries, caused by endothelial cells and pericytes [24], as well as by intravital microscopic observations in his own institute, the author came to his ideas on the cell physiology of the switching mechanism of the microcirculation [25] shown roughly and schematically in Fig. 1. It is assumed here that reversible changes in form, and swellings of the vessel wall cells (endothelial cells, pericytes, which are dependent on the degree of their O_2 supply) influence the narrowest inner cross-section of the capillaries. This assumption is in harmony with old experimental findings on the transformation from an elongated to a spherical cell form (epithelial cells) in ATP deficiency [26]. Electron micrographs produced direct pictures of the narrowing of capillaries due to swelling of endothelial cells in energy or O_2 deficiency (hypoxia). The picture in Fig. 2, taken from Loewe and co-workers [27], shows the stage of initial swelling of the endothelial cell. It can be seen

Primary O_2 deficiency causes an O_2 (energy) deficit in the wall cells at the venous capillary end, which then swell and thereby lead to a narrowing of the vessel with reduced bloodflow.



Narrowing of vessel

intensifies the above-mentioned O_2 deficiency by:

1. *Reduced bloodflow Q*
2. *Increased apparent blood viscosity*

Therefore a system with a switching property (change-over when a threshold level is exceeded). The change-over threshold is determined by the level of the venous pO_2 and its duration of influence as well as by the blood flow intensity.

Fig. 1 Ideas for the triggering of the switching mechanism of the blood microcirculation at the venous end of the capillaries in O_2 deficiency

[1] H_2O flows into the cells as a consequence of the failure of the K^+/Na^+ pump, which requires a great deal of energy

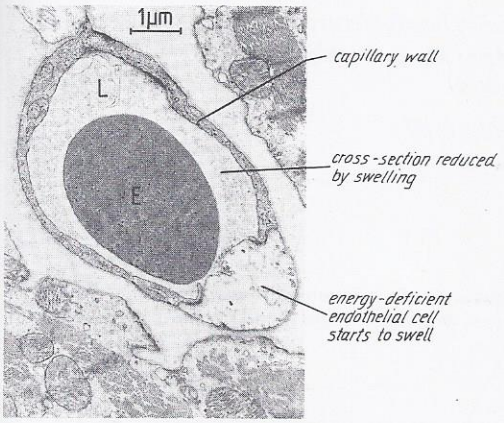


Fig. 2 The elementary process of the switching and regulating mechanism of the blood microcirculation at the venous end of the capillaries in the electronmicroscopic picture. (Loewe et al. [24]. It was discovered that these swellings of the endothelial cells, if not yet at too advanced a stage, can be *lastingly* reduced by O_2MT procedures. Blood microcirculation strengthened in all perfused capillaries of the organism, weakened in distress. L = capillary lumen; E = erythrocyte

from further photographs and measurements that there is always a transition to total occlusion by the swelling of the capillary endothelium. We could derive from P_{O_2} measurements that, up to a certain intermediate stage, the *switching mechanism remains reversible, and this is the area of influence of the O_2 multistep procedures*. Here it should be noted that, according to the P_{O_2} course between the arterial and venous ends of a capillary shown in Fig. 3, the bioenergetic control of the narrowest capillary cross-section is to be expected primarily near the venous end of the capillary, because the lowest P_{O_2} levels are to be found there. A high proportion of the cell energy serves the maintenance of the sodium pump (Na^+/K^+-ATPase, osmoregulation of the cell). In energy deficiency in the wall cells at the venous capillary end, a reduction in the pump performance occurs and, with it, an accumulation of hydrated sodium ions [28]. The swelling which then occurs can be removed by the restoration of a good energy situation (high $P_{O_{2\text{-ven}}}$). Further details of the pathophysiology of the endothelial cells can be found in [29, 30] and in the literature references 4 to 6 in [27].

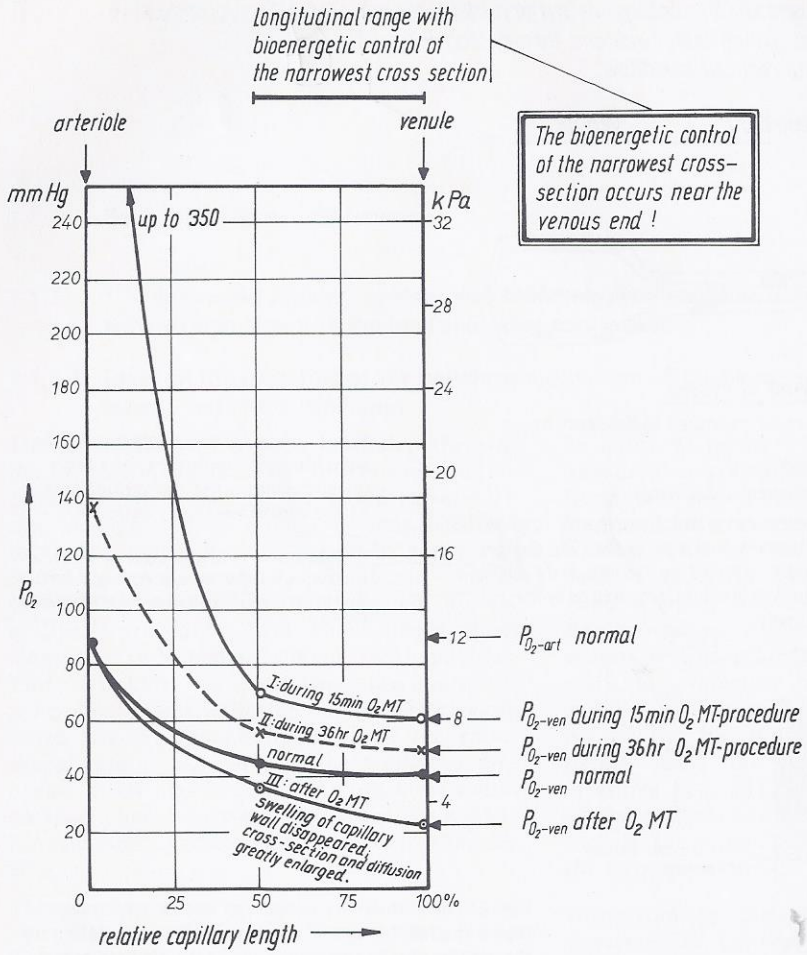


Fig. 3 Example of P_{O_2} courses between the arterial and venous ends of a capillary during a 15 min O_2MT procedure (II), and after O_2MT (III). The values of $P_{O_{2\text{-ven}}}$ increase with $P_{O_{2\text{-art}}}$ and blood flow in the envisaged capillary under O_2 application of O_2MT treatment

In order to explain the long-lasting effect, i.e. to justify the interpretation that we are dealing with a real switching process, it is necessary to show that, in the bioenergetic control of the narrowest capillary cross-section, it is a *system with feedback*. This can be immediately recognized when we remember, for example, that the primarily poor O_2 supply situation leads, via the triggered narrowing of the cross-section with a drop in the blood microcirculation, to a further significant deterioration in the O_2 supply. The deterioration is even further intensified because the apparent blood viscosity increases as a result of a reduction in the shear stress in the blood flow, as in Fig. 4. This chain of deteriorations in the O_2 supply signifies the *existence of a system with positive feedback*. Such systems have, as is generally known, the property of bringing about a change in quality by an accumulation of quantitative elements. They have *switching properties* when a certain degree of feedback is crossed. Beneath this switching threshold there is only a control with a greater or lesser enhancement effect, but this is not of any duration. It can thus be understood that, in the implementation of the O_2 multistep procedure, a certain threshold of the oxygen dosage applied must be crossed, in order to maintain the high η^+-effect for a long period of time. In Table 1 there is a compilation of the characteristics of the bioenergetic control dose for the "switching" or "regulating" areas, and the procedure variants discussed below. The same distinction also applies

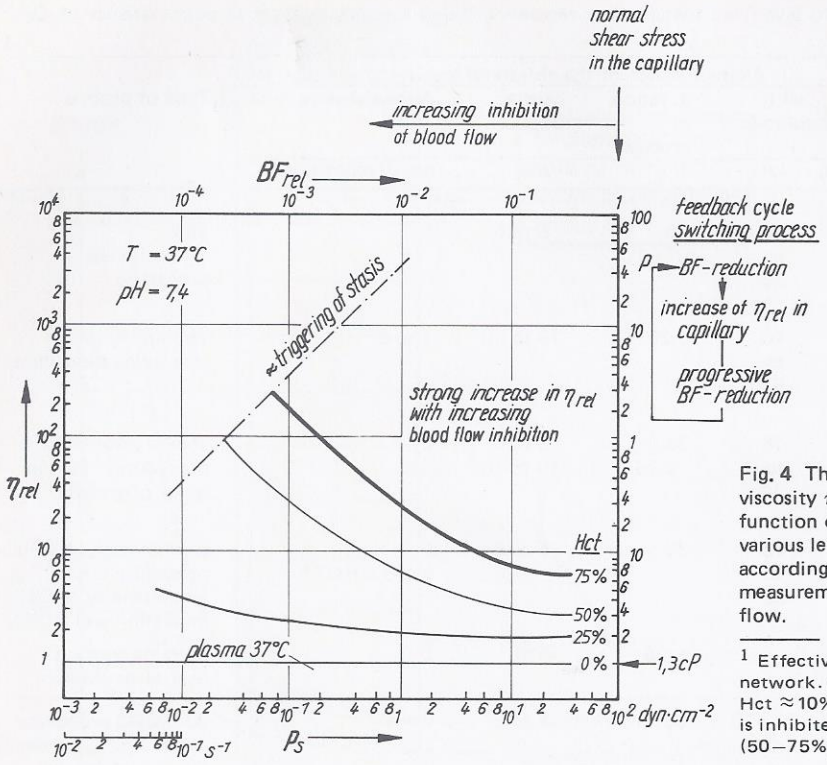


Fig. 4 The relative apparent blood viscosity η_{rel} in larger vessels as a function of the shear stress p_s for various levels of the hematocrit Hct according to Schmid-Schönbein's measurements [31]. BF = blood flow.

[1] Effective hematocrits in terminal network. Normal conditions: Hct ≈ 10%. When microcirculation is inhibited, Hct becomes very high (50–75%)

1.1.1.2 Differences in the triggering of the switching mechanism in the various organs and tissues. Relationship to the degree of effectiveness of the O_2 multistep therapy procedures

Differences in the consequences of O_2 deficiency condition in various organs and tissues of the human body on the one hand, and the observed differences in the response for the elimination of O_2 deficiency on the other, stimulated us to investigate the (common) cause for these differences. The cause was thought to lie in a *varying level of the switching threshold of the bioenergetically controlled switching mechanism of the blood microcirculation*. The effect of this mechanism, which occurs generally in the whole body, simultaneously and equidirectionally, is superimposed onto the local regulation processes of the microcirculation, e.g. through precapillary sphincters [32], which have been known and thoroughly investigated for a long time.

At the venous end of the capillaries, where the lowest P_{O_2} level exists, the endothelial cells of the capillary wall begin to swell due to water absorption in O_2 deficiency, because the K^+/Na^+ pump, which demands roughly 30% of cell energy, diminishes in its performance [34]. The swelling leads to the cross-sectional narrowing already discussed and, after the switching threshold is crossed, to the triggering of the switching mechanism.

The swelling of the endothelial cells in O_2 deficiency is at first of a *reversible nature*, which means that the detumescence of the wall cells and, with it, a renormalization of the reduced blood microcirculation can be achieved by the production of high P_{O_2} levels at the venous capillary end (and of an increased capillary blood flow, e.g. by means of physical exertion) over a certain length of time (detumescence time). The further research into the parameters governing these dynamics is one of the most interesting tasks of the field of microcirculation, as the *switching and regulating mechanism* described *seems to be representative for the uniform initial process in myocardial infarction*, in *shock*, in *peripheral circulatory disorders*, in *damage caused by distress* etc., as well as, in the opposite direction (which greatly upgrades the microcirculation) in *sports stamina training*, and in the *procedure variants of oxygen multistep therapy*.

The *duration time for the high-charging of a downgraded microcirculation* (detumescence time) is *determined by the therapeutically applied P_{O_2} level at the venous capillary end.* The O_2 supply of the endothelial cells at the capillary end by means of diffusion is dependent on this. From the measurements of this in Fig. 3 (guiding values) it emerges that, with the procedure variant with increase in cardiac output by means of severe physical exertion and $P_{O_{2\text{-ven}}}$ = 60 mmHg (8 kPa) the threshold for high-charging will be crossed with sufficient certainty in 15 min; with the procedure variant without increase in cardiac output, and $P_{O_{2\text{-ven}}}$ = 45–50 mmHg (6–6.6 kPa) in approximately 36 h.

The aforementioned $P_{O_{2\text{-ven}}}$ levels are attained using the *standard 15 min O_2 multistep quick procedure* discussed below, and the standard *36 h/18 day O_2 multistep procedure.*

From the theory of diffusion and from experimental experiences there results the following *relationship for the effectiveness W of O_2 multistep therapy procedures* and of procedures of hyperbaric O_2 multistep therapy:

$$W \sim (P_{O_{2\text{-ven procedure}}} - P_{O_{2\text{-ven before}}})^n \cdot t_{procedure}$$

Key:

$P_{O_{2\text{-ven procedure}}}$ = venous P_{O_2}, measured during procedure with O_2 application. This value is dependent on the arterial P_{O_2} during the procedure and the bloodflow Q in the capillaries. The Q-level is roughly proportional to the cardiac output and therefore approximately twice as high during the 15 min procedure as in the 36 h procedure. *The strength of the microcirculation therefore has a significant influence on the triggering of the switching mechanism.*[1]

$P_{O_{2\text{-ven before}}}$ = venous P_{O_2}, measured before procedure

n = efficiency exponent ≈ 3.5; empirically obtained from the measured values in Fig. 3[2] and the relationship of the duration of procedures

$t_{procedure}$ = total duration of the O_2MT procedure

If, due to the named procedure variants or due to their reversal in the direction of "O_2 deficiency conditions over a certain length of time", the oxygen partial pressure simultaneously changes at the venous end of all capillaries of the organism over a certain time span, a comprehensive effect occurs. It can be measured absolutely by spirometry as a *change* in the resting O_2 uptake or CO_2 production of the organism. Relative values of this change can be gained from changes in the arterial and venous resting P_{O_2} (see Section 1.1.5).

In the framework of the application of the O_2MT it is usually only the total effect that is considered in the judgement of the O_2 situation and its dynamics. A more detailed evaluation was made in [35].

It is known that the O_2 utilization varies greatly, dependent on the rate of O_2 consumption in the individual organs and tissues. This has as a result that the venous P_{O_2} of the various organs and tissues shows great differences. The *scale of $P_{O_{2\text{-ven}}}$ levels for normal young persons*, resting, is given in Fig. 5 B, bottom row. It reaches 22 mmHg (heart) to 68 mmHg (spleen). The mixed blood carried to the lung has a resting $P_{O_{2\text{-ven}}}$ level of 40 mmHg, with physical rest and compensated cardiac output.

It is known that the mixed $P_{O_{2\text{-ven}}}$ at rest decreases to roughly 35 mmHg in old age [35]. The reduction is obviously a counter-regulation of nature, to counter the severe drop of the arterial resting P_{O_2} in old age [37]. Corresponding to the reduction of the mixed $P_{O_{2\text{-ven}}}$ of an average 5 mmHg at an age of 75 years, roughly the same reduction of the resting $P_{O_{2\text{-ven}}}$ levels assigned to the organs and tissues occurs. The scale of the expected resting $P_{O_{2\text{-ven}}}$ levels for older, untreated persons is given in Fig. 5 B, top row.

The O_2 supply to the endothelial cells at the venous capillary end depends on the level of the venous O_2 partial pressure. A high $P_{O_{2\text{-ven}}}$ results when a high arterial O_2 partial pressure is

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[1] The effect contribution of the optional adjuvant steps of *HOT** and *hemodilution* is mainly reflected in an increase of blood flow Q.

[2] $P_{O_{2\text{-ven procedure}}}$ = 45 mmHg assumed for the 36 h procedure

produced (O_2MT procedure with high O_2 offer to the lung, adapted to the respiration minute volume RMV) and when there is a high capillary blood flow Q (high cardiac output, physical exertion). The strength of the blood microcirculation therefore plays a significant role in the *triggering of the switching mechanism of the microcirculation*. The reason why a reduction of the microcirculation (cardiac infarction, intermittent claudication) occurs more frequently in older persons may be considered to lie particularly in the decrease in the nutritive capillary blood flow (reduction of cardiac output with age [37]) and thereby in the $P_{O_{2\text{-ven}}}$.

According to these explanations, the scale of the resting P_{O_2} of the various organs and tissues (Fig. 5 B) gives us a clue to the *mean risk for the various organs and tissues in O_2 deficiency* (old age [37], stressful influences [20, 21]. According to this compromise of the heart (myocardiac infarction) could first be expected in O_2 deficiency, due to diminishing of the microcirculation, and then in the lower extremities, and also in the brain (circulatory disorders, dizziness) and in the eyes. Correspondingly it is to be expected that an *improvement of the O_2 status with procedure variants of the oxygen multistep therapy or stamina training*, will *help* first the heart, then the lower extremities, as well as the brain (circulatory disorders) and the eyes. The above formulated rules give us new insights into the multifactorial process in various important diseases, suffering and complaints based on O_2 deficiency.

Due to the discovered correlation between the quality of the O_2 status and the strength of the host's cellular defense capacity [18], *significant local differences in the strength of the defense capacity dependent on location*, can be *expected in the human organism from this viewpoint*. This assessment carries more weight when we begin to take into account the local variations in the defense cell density (differences in the parameters of the capillary network and the microcirculation etc.). Cancer tumors can be expected to manifest themselves more frequently in parts of the organism where local minima in the O_2 status and in the defense cell density have existed over a certain period of time. It is particularly easy to recognize O_2 status minima in the area of the skin, e.g. by means of transcutaneous large area measurement of the P_{O_2}. Skin abnormalities often form the grounds of such minima, which can be made to disappear or at least to weaken by oxygen multistep stimulation of the host's defense. Investigations of this type lead to an interesting dermatological research area.

The peripheral circulatory disorders in the lower extremities, caused by a deterioration in the O_2 status and often ending in the necessity of a leg amputation, are among the commonest illnesses of old age. This fact can be explained by the low level of the resting $P_{O_{2\text{-ven}}}$ measured in a standing position, of this area of the skeletal musculature, already discussed (see also Fig. 5 B), combined with the drop in the resting O_2 uptake of the organism, or of the cardiac output, to a level at the age of 75 years of 65 % or 62 %, relative to the maximum (30 years).

In order to round off our ideas, it seemed necessary to find an answer to the question of why this disease affects primarily the lower, and not the upper, extremities, and why O_2 multistep therapy (and also HOT-UVR therapy) usually gives unique aid particularly in circulatory disorders of the lower extremities (Fig. 5 A). In order to answer these questions, *measurements of the resting $P_{O_{2\text{-ven}}}$ at the upper and lower extremities* were undertaken, *in a standing position*, the mean levels of which can be found in Fig. 5 B. As our ideas had led us to expect, it was found that the *venous resting P_{O_2} in the lower extremity is significantly lower that in the upper* (measurement in a standing position), by 7 mmHg/0.93 kPa). This result explains the preference of the lower extremities in the pathogenic decharging of the microcirculation in the skeletal musculature, and in the therapeutic high-charging.

Within the framework of these investigations we gained information about the course of the venous resting P_{O_2} and the blood microcirculation in the lower extremities during the pathogenic and therapeutic processes, summarized in Fig. 6. It may seem disconcerting at first that a poor O_2 supply to the capillary wall cells can exist with a high level of the local mixed $P_{O_{2\text{-ven}}}$ (Fig. 6 C) and conversely, that the best O_2 supply (Fig. 6 E) can occur with a particularly low level of the local mixed $P_{O_{2\text{-ven}}}$. These paradoxical findings can be explained by a change in the diffusion areas as a function of the nutritive blood flow Q, which is very low in the first case and very high in the second (see also the above relationship of the effectiveness of O_2MT procedures). The dynamics of the microcirculation also contribute to the fact that, in the $P_{O_{2\text{-ven}}}$ control of the discovered witching mechanism, the $P_{O_{2\text{-ven}}}$ levels of the switching threshold for the lowering or raising of the microcirculation are very far apart (Fig. 6, right).

The *physical handicap* occurring due to peripheral circulatory disorders usually leads to a lifestyle lacking in exercise. According to [20, 21] *long term physical inactivity is one of the stressful influences causing a particularly severe deterioration of the O_2 status*. The resultant lack of exercise therefore has as a consequence an intensification of the O_2 deficiency which triggers the reduction of the microcirculation. This vicious circle causes a *particularly stabile consolidation of this detrimental state*: the nutritive capillary perfusion succumbs almost completely. For this reason an *intensive variant of the oxygen multistep therapy* is usually used to combat peripheral circulatory disorders in the lower extremities, in which the standard O_2MT procedure is combined with a HOT-UVR treatment, which favors the switching process. This intensive variant has already been used against circulatory disorders of the lower extremities in many cases in the now more than 300 centres for oxygen multistep therapy treatment. Numerous successful treatment results have been gained: patients who had for years burdened those around them as severe nursing cases, left heir beds and returned to a life with physical exertion; after the O_2MT, the reduced temperature of the leg was frequently raised to a normal level, and an already planned amputation could be avoided; in almost all treatments in the early stages of this disease there resulted an extremely impressive increase in pain-free walking distances.

We have selected this particular problem and its combat by means of O_2MT procedures as a classic example, with the intention of presenting a pathogenic process which has the *specific characteristic that it causes an additional deterioration of the O_2 status of the organism, due to the lack of movement caused by the problem itself*.

1.1.2 The O_2 partial pressure and the proportion physically dissolved in the blood during and after O_2 multistep therapy

The bioenergetic control of the switching mechanism of the microcirculation, already mentioned, occurs due to the proportion of oxygen physically dissolved in the blood. Although this proportion is very small, compared with the proportion chemically bound to the hemoglobin, it alone is able to react and is therefore effective. The physically dissolved oxygen is kept at an even level by means of immediate transport from the O_2 fraction chemically bound to the hemoglobin. The *volume of the physically dissolved O_2 fraction in the blood as a function of the oxygen partial pressure* can be taken from Fig. 7. The pressure areas for the arterial and venous P_{O_2}, existing *during* and after O_2MT multistep therapy procedures, can also be found there. The measured temporary increase in the P_{O_2} levels near the venous end of the capillary (see also Fig. 3) *during* the O_2 multistep therapy procedures is decisive for the triggering of the switching mechanism of the microcirculation. This *temporary large increase in the P_{O_2} at the venous end of the capillary* naturally particularly benefits the endothelial cells which are located there and are decisive for our procedure. The increase in the P_{O_2} at the venous capillary end is favoured when the circulation of the lung and heart is simultaneously significantly increased by means of physical exertion, as in the 15 min O_2 multistep quick procedure. In the 36 h O_2 multistep procedure an increase is achieved in the P_{O_2} at the venous capillary end just sufficient for the triggering of the switching process, when $P_{O_{2\text{-art}}} > 125$ mmHg (16.6 kPa) is measured under O_2 inhalation.

The increases in the arterial P_{O_2} during the O_2 multistep procedures (see Fig. 7) only lead to a directly proportional increase in the O_2 diffusion into the tissue in a few areas of the organism. In these few areas, where the course of saturation in the upper part of the O_2 binding curve of the blood does not limit the effects, particularly strong effects of O_2 multistep therapy can be expected and also observed. The *functional elements of lung bordering the alveolar space* can be named here; also *the vessel walls of the arterioles or arteries*, which receive their oxygen, not through the vasa vasorum, but solely, or to a large extent, through diffusion from the relatively large vessel volume. Further examples of this type are the lens of the eye, the cartilage and the vocal chords. Almost all other tissues of the organism receive oxygen via capillaries, the O_2 transport function of the hemoglobin, discussed in the following section, thereby gaining decisive significance.

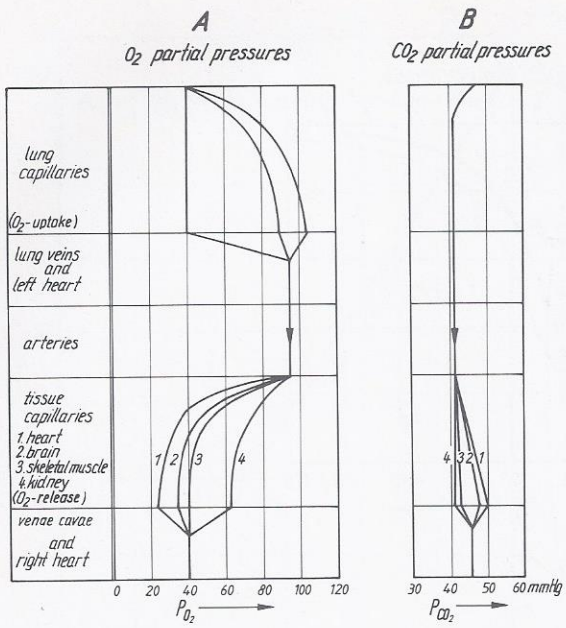

Fig. 9 O_2 partial pressures (A) and CO_2 partial pressures (B) of the blood in the various sections of the circulatory system under resting conditions

on chemical [16] or other ways to overcome the membrane barrier, without losing the IHP effect [45]. Because of its complicated nature and the fact that it is effective for only 60 days, this method has not as yet been of practical significance. It should be pointed out in this section that, according to [46], the DPG concentration in erythrocytes is increased by roughly 20 % by intensive physical training. Next to the slight shifting of the O_2 equilibrium curve to the right, caused by this, a flattening of the curve and an increased venous resting P_{O_2} can be observed in competitive sportsmen.

1.1.5 The determination of the resting O_2 status and further characteristic values

1.1.5.1 Definition of the resting O_2 status

The *absolute characteristic value for the resting O_2 status* be defined as the spirometrically determined O_2 absorption of the organism via the lung under conditions of physical rest. Strictly speaking, the O_2 absorption is given as the sum of the two contributions Q_{O_2} and Q'_{O_2}, with Q_{O_2} representing the O_2 transport to the organs and tissues by means of O_2 loading and O_2 discharging of the hemoglobin in the blood circulation, and Q'_{O_2} representing the O_2 transport by direct O_2 diffusion from the lumen of the arterial vessels to special tissues (e.g. arterial walls, vitreous body, cartilage, etc.). As $Q'_{O_2} \leqslant Q_{O_2}$, it is generally sufficient for consideration of the balance, to use Q_{O_2} alone as an (absolute) characteristic value for the resting O_2 status.

The numerical value of Q_{O_2} is, according to Table 2, a product of three factors. Fast and great fluctuations are only observed in the first factor, the *O_2 saturation difference* η of the blood. The momentary *resting level of η is therefore a relative characteristic value for the momentary O_2 status, with information content of high diagnostic significance.*

The second factor, the *resting cardiac output* normally changes only slowly with training condition and age.

The third factor, the *hemoglobin content* Hb of the blood usually remains roughly constant in the individual case, also over longer timespans.[1]

[1] The hemoglobin content is known to be temporarily reduced to roughly 66 % of its starting level, with the hemodilution method [47]. Nevertheless, a significant increase in the O_2 transport to the body tissue results, particularly because the venous P_{O_2} drops, and the great increase in η and in cardiac output which then occur, greatly overcompensate for the influence of the hemoglobin (hematocrit) reduction.

1.1.5.2 Time of day for determination

The absolute characteristic value Q_{O_2} and the relative characteristic value η of the resting O_2 status change significantly in the course of the circadian cycle. Figure **10** A shows a measurement example of η for this. In Fig. **10** B our measurement is compared with the circadian rhythm of the mean disposition to work, according to O. Graf [48]. For the establishment of the therapy effect, the resting Q_{O_2} or resting η measurements before and after treatment should always be undertaken at the same time of day (and under the same external conditions). We recommend the *standard measurement* to be taken at 15.00 hours (14.00–16.00 hours), at rest and in a sitting position, representative for the approximate *minimal level between morning and evening*. An early measurement at 9.30 hours (7.00–9.30 hours), accomplished under the above-mentioned conditions, seems to be representative for the maximal level between morning and evening.

If the unique opportunities, which lie in the determination of the resting O_2 status for diagnostic purposes, are to be used, it is particularly important to standardize the time of day for the determination (e.g. 14.00–16.00 hours).

The deep minimum of the O_2 status approximately 3 h after falling asleep is noteworthy in Fig. **10**. It is the time point at which circulatory disorders, cardiac arrest, myocardiac infarction in risk patients occur with greater frequency. The low level of this nightly minimum can usually be somewhat countered by a cup of strong coffee immediately before falling asleep [49], and strongly countered by a lasting improvement in the O_2 status with the aid of the oxygen multistep therapy.

1.1.5.3 Determination of the arteriovenous saturation difference η at rest as a relative characteristic value of the O_2 status

The determination of the η level is one of the most frequent and most important tasks in the use of the results compiled in this book. It has the advantage that it also shows the resting levels of the arterial and venous P_{O_2}, which are often highly meaningful on their own. *The determination of the relative characteristic value* η is usually sufficient to make a diagnostic assessment of the patient's energetic reserves, to record the consequence of stress, to document therapy results and to decide whether a repetition of the therapy is necessary.

By measurement of the arterial and venous P_{O_2} in conditions of rest, the two working points on the HbO_2 dissociation curve of the blood shown in Fig. **11** for normal conditions (T = 37 °C, pH = 7.4), are determined. The *utilization factor of the O_2 binding capacity of the blood* (O_2 saturation difference) in each case can be seen from the position of the working points. Five examples of the positions of the working points and η-values before (0, 1, 2) and after (3, 4) implementation of the O_2 multistep procedures are shown in this presentation. Help is given in Fig. **12** in the form of a *nomogram for the determination of the factor η of the O_2 binding capacity* of the blood, dependent on $P_{O_{2\text{-art}}}$ for various levels of the mixed central $P_{O_{2\text{-ven}}}$.

The cardiac output (COP) is the product of the stroke volume V_s and the pulse frequency f. In resting conditions the stroke volume remains virtually uninfluenced. The naturel *counter-regulation* in η-changes almost exclusively takes the form of *adaptation of the pulse frequency*. It is therefore usually sufficient for the stricter assessment of the relative O_2 transportation, to know the value of the relative pulse change

$$k_f = \frac{f + \Delta f}{f}$$ in the corresponding change of η.

Measurements of the η/pulse counter-regulation after O_2 multistep therapy are summarized in Fig. **13**. The measured relative drop in the pulse only reaches a level of $k_f = 0.91$, even after a tripling of the η-value. *The η-value therefore largely determines the volume of the O_2 transport to the body tissue under normal conditions*. With this approximation, further discussion may be limited, as a rule, to the consideration of the η value and its dynamics. Only in conditions of weakness with very (too) low η-values (< 15 %) is it necessary to take into account the fact that the organism then reacts for a limited time with a significant increase in the cardiac output (increase in pulse frequency) in order to ensure a level of O_2 transportation Q_{O_2} that is just adequate. Examples of this are cases 8 and 10 shown in Fig. **15**.

Although the methods and techniques of determining the arterial and venous P_{O_2} are discussed in depth later in the book, it seems necessary to mention at this stage the hitherto apparent principle difficulties. The sufficiently accurate measurement of the resting $P_{O_{2\text{-art}}}$ is today problem free, usually made from a drop

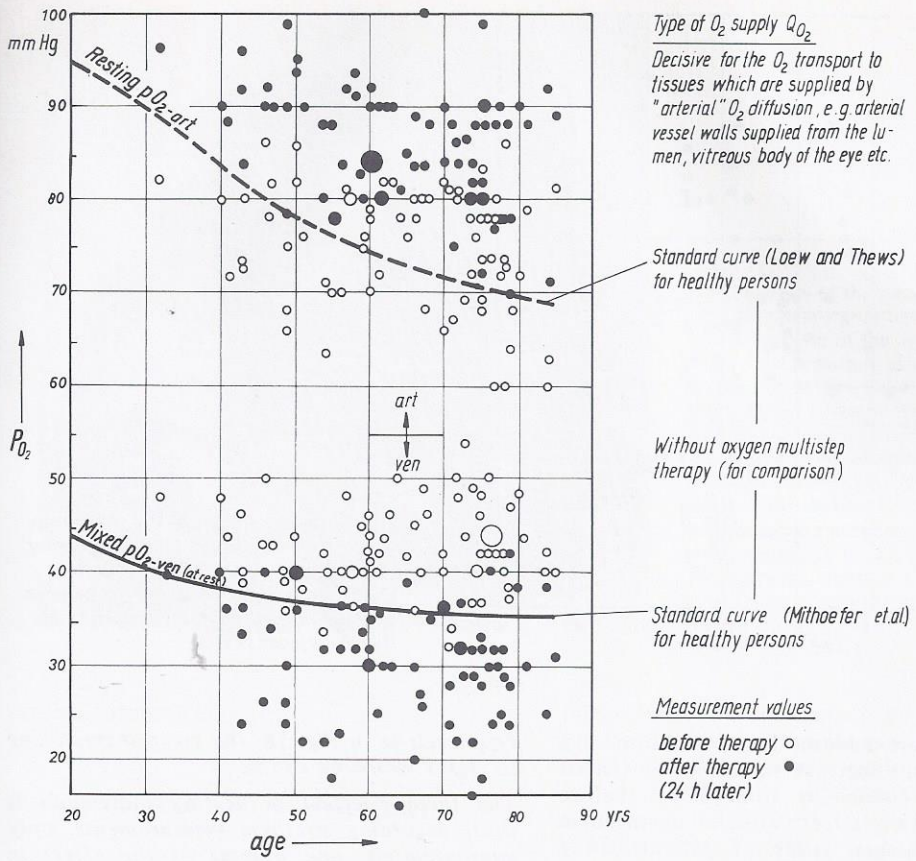

Fig. **18** Measurements of the arterial and venous oxygen partial pressure before and after oxygen multistep therapy (usually variant GK 4-I), dependent on age, in patients in need of treatment at the sanatorium of Dr. H. Wolf, Bad Wildungen, FRG. Results of 72 successful treatments. Number of failed treatments: 8 (= 11%). Measured values in comparison to the expected values (standard curves according to Loew and Thews and Mithoefer, respectively). Increased η (O_2 uptake at rest) by means of therapy from 100 to 230% (80 patients; 1985). The increase in the O_2 uptake, or in the CO_2 release, is approximately half of the increase in the value of η (see appendix)

jectively strongest effects of the O_2MT are not to be expected in individuals in full possession of their physical strength, but in weakened, ill or suffering patients.

Studies on the effect of O_2 multistep therapy should therefore be performed on physically weakened subjects[1], e.g. on patients in clinics and sanatoria. This view is confirmed by the measurements and the course of the two expected curves in Fig. 18. Both fields here, with the values measured *before* therapy, both below ($P_{O_2\text{-art}}$) or above ($P_{O_2\text{-ven}}$) the respective expected curves (with their in places very high levels of the resting $P_{O_2\text{-ven}}$), are an expression of the weakened condition of most patients studied. Fascinatingly, it can be seen here that after O_2MT treatment the measured values for nearly all age groups can on average be found to be way above ($P_{O_2\text{-art}}$) or way below ($P_{O_2\text{-ven}}$) the respective expected curve. The mean increase in the $P_{O_2\text{-art}}$ here is approximately 10–20 mmHg (1.4–2.8 kPa), whilst the mean reduction of the resting $P_{O_2\text{-ven}}$ is approximately 10–15 mmHg (1.4–2.1 kPa). *A very significant increase in the O_2 status (η-value) of the patients is reflected in these numbers*, correlating with impressive records of objective and subjective improvements in the condition of health of the individual patients. Almost the same results, admittedly with a smaller number

[1] But not on permanently bedridden patients who are incapable of sufficient movement (lack of the 3rd step of therapy; for such patients, HOT* is indicated as an adjuvant step)

Fig. **20** View of the measuring assembly for the determination of the O_2 uptake at rest and of the maximal O_2 uptake of the organism, as well as of CO_2 production at rest. Development: Manfred von Ardenne Research Institute. Simultaneously with our own development, an Oxycon-4 instrument from the Fa. Hellige, Freiburg/Br. (FRG) was put into operation in order to record the measured values of the lasting great increase in the O_2 absorption of the organism, and of the CO_2 emission after O_2 multistep therapy as given in the appendix

$$\text{cardiac output (COP)}_{[l \cdot min^{-1}]} = \frac{\text{resting } O_2 \text{ uptake } [l \cdot min^{-1}]}{\eta \cdot 0.2144_{[O_2]}}$$

The value of η is determined immediately after measurement of the O_2 uptake, in order to exclude the possibility of errors due to the discovered circadian rhythms in the 24 h cycle (Fig. **10**). If the Hb value of the patient is known, the product of the individual Hb and the factor $1.34_{[ml\ O_2\ per\ g\ Hb]}$ should be used instead of the coefficient 0.2144. The standard measurement of 15.00 (between 14.00 and 16.00 hours), resting and sitting, roughly represents the *minimal level* between norning and evening. The early measurement at 9.30 (between 7.00 and 9.30 hours), resting and sitting, is roughly representative for the *peak level* between morning and evening.

Figure **21** A shows typical examples of the increase in the O_2 uptake at rest due to the 36 h 18 day O_2MT procedure discussed below, both without (variant GK 4-I) and with cardiac training (variant GK 4-II).

The extent of the contributions of the increase in O_2 uptake under various conditions can be taken from the spirometric measurements of the uptake in Fig. **21** A (cases of untreated persons and volunteers previously O_2MT treated without and with cardiopulmonal minimal training included in the study). In the case examined there resulted for the male aged 77 years through O_2MT alone a lasting increase of the O_2 uptake to 161 % and through O_2MT with cardiac training, an increase in the O_2 uptake to 188 %. According to Fig. **19** B, the arteriovenous O_2 saturation difference η increased to 209 % due to O_2MT with cardiac training. The improvements in pulse frequency, stroke volume and COP by the two O_2MT variants can be seen from Figs **21** C, D and E.

Towards the end of the 36 h 18 day treatment (O_2MT and heart training) the curves in Figs **21** A, B, D and E show the shift of the operating point into a range with saturation character. It can be concluded from this that the chosen combination of type and dosage of the cardiopulmonal minimal training (O_2, Alupent, physical exertion without extra O_2) have been successful in achieving the desired training effect in the heart without further time expenditure in the framework of the *36 h 18 day O_2MT standard procedure*.

1.1.5.5 Determining the maximal O_2 uptake as a characteristic value of the energetic reserves of the organism

The maximal oxygen uptake is an indicator, used particularly in sports medicine, of the aerobic *performance capacity* of the organism. It is measured when the individual is subjected to continuously increasing strain with an ergometer. When the state of exhaustion is reached, the oxygen uptake levels off. The numerical value of O_2 uptake in the plateau phase is an indicator of the maximum O_2 uptake or of stamina performance capacity. This figure is diagnostically very informative, as it can also be seen as a kind of *characteristic value of the energetic reserves* of the organism. It would therefore be desirable for measurement devices for the routine determination of the resting O_2 uptake and the maximal O_2 uptake to go into large-scale production in the not too distant future.

The expected curve for the maximal O_2 uptake QO_2-max dependent on age in normal persons can be seen in Fig. **22**. The course of the curve shows that this characteristic value drops continuously and steeply after the age of about 20. At the age of 80 the figure is only approximately 42% of the maximum in youth. The closed circles entered give an idea of the mean variation, and the points marked with a cross were obtained from senior sportsmen. It can clearly be seen that the reduction in the maximal O_2 uptake occurs much more slowly in elderly, physically active persons than in normal persons. The documented result is a serious warning to able-bodied persons not to neglect regular training (cardiovascular training) even in later years [58].

The lower part of the same figure shows the *expected curve for the resting O_2 uptake dependent on age*. On the basis of the level of the youthful age of 20–25 years, a drop in the resting O_2 uptake, e.g. at the age of 80, of approximately 62% can be seen. In physically active persons of the same age group, the respective value drops to about 60–70% of the maximum. At the bottom of the same figure, measurements of the resting O_2 uptake after implementation of the O_2MT have been entered as typical examples.

It seemed advisable for practical reasons to design the measuring set-up in such a way that both the maximal and the resting O_2 uptake could be measured by the same apparatus. This

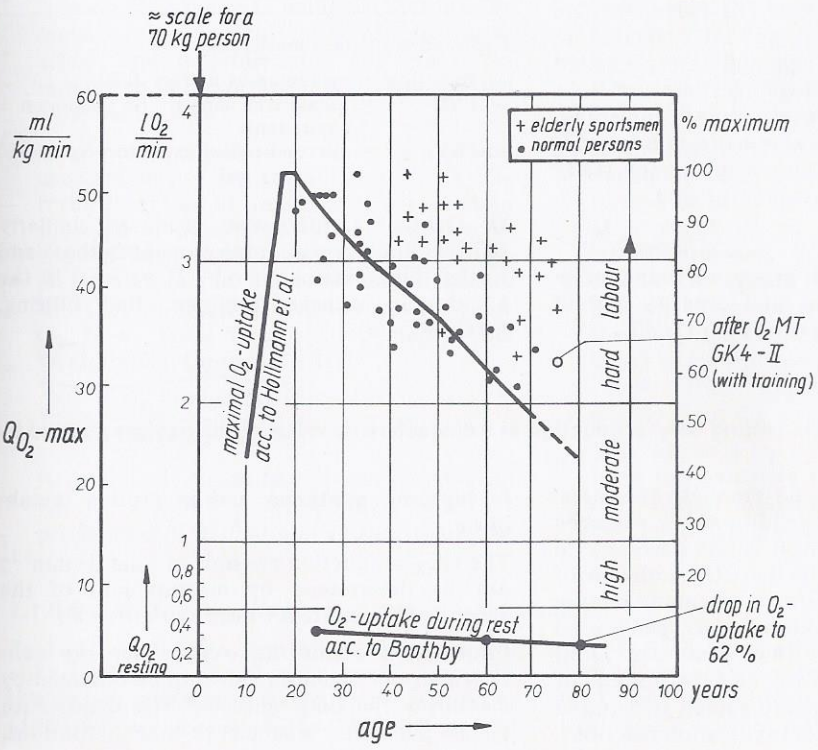

Fig. **22** Maximal O_2 uptake Q_{O_2}max as characteristic value of the cardiopulmonal system dependent on age, for normal persons and elderly sportsmen acc. to Strauzenberg as well as resting O_2 absorption and Q_{O_2} at rest (STPD conditions) dependent on age for a normal person calculated acc. to [48] and O_2MT patients

was achieved in the arrangement shown above by the use of a flow sensor covering the range from 0.12 to 20 l/s. In addition, the flow channels were designed with an inner diameter of more than 20 mm in order to keep the flow resistance sufficiently low, even in flow peaks.

1.1.5.6 Determining the lung function parameters

Pneumologists (Petro, Daum) were, as quoted in [17], of the opinion that the oxygen multistep therapy procedures could not bring about a lasting improvement of the parameters of lung function [59] ('None of these partial functions of respiration can be changed in any way by the exogenous supply of oxygen'). This standpoint was opposed by the author's expectation that, by means of the high-charging of the blood microcirculation in the lung area also, and the lasting improvement in the energetic status (an increase in the performance capacity of the respiratory musculature), a long-term improvement in the parameters of lung function does or can occur. In order to settle this question a pilot study was performed, at first by Dr Gabriele Caspers and finally by us. For this a Spiroton-2 device from the Drägerwerk, Lübeck, FRG, was used, made available by the courtesy of the Erwin Braun Institute of Preventive Medicine, Engelberg, Switzerland. This instrument determines from a single expiratory breath, which can be repeated twice after an adequate interval, the parameters exemplified in the two following cases. The parameters are retrieved from a memory and are evaluated inside the instrument. The results are presented by a plotter as flow and volume/time curves. In this way the following results were documented, showing that *lasting improvements in lung parameters due to* oxygen multistep therapy really can be objectified (see column, right).

In 15 patients from our group we found an increase of 6.5% in the vital capacity and of 15.4% in the peak flow (PF) after O_2MT.

Case 1: 24-year-old male patient with functional vegetative complaints. Treatment: two 15 min O_2MT quick procedures

Parameter	before	after O_2MT	Difference absolute	relative
Peak flow [$l \cdot s^{-1}$]	8.21	10.50	+ 2.29	+ 28%
FVC [l]	5.27	6.04	+ 0.77	+ 15%
FEV_1 [l]	4.28	4.26	- 0.02	0%

Case 2: 54-year-old male patient with obstructive ventilation disorder. Treatment: 36 h 18 day O_2MT procedure

Parameter	before	after O_2MT	Difference absolute	relative
Peak flow [$l \cdot s^{-1}$]	4.68	5.81	+ 1.13	+ 24%
FVC [l]	3.39	3.60	+ 0.21	+ 6%
FEV_1 [l]	1.87	2.08	+ 0.21	+ 11%

Explanation of the abbreviations:

- Peak flow = maximum expiratory flow
- FVC = forced vital capacity (in maximum expiration)
- FEV_1 = 1-second forced expiratory volume; Tiffeneau test

Dr Gabriele Caspers also produced similarly positive findings with improvement in these and further lung parameters on 171 patients in the Klinik für Naturheilverfahren, Bad Füssing, FRG [60, 400a].

1.1.5.7 Determining the resting CO_2 production as a characteristic value of the oxygen utilized by the organism

In order to be able to differentiate the metabolic pathways of the (additionally) absorbed oxygen in the organism, it is also necessary to determine quantitatively the CO_2 emission of the lungs. Figure 23 shows a schematic picture of these pathways. The absorbed oxygen is used for energy production (biological oxidation) in the respiratory chain of the mitochondria of all cells. Part of the energy gained is required for immune processes, detoxification reactions, in hormone syntheses and in protein metabolism.

The CO_2 production per unit of time ($l \cdot min^{-1}$) can be determined by measurement of the absolute CO_2 content of the expiration air.

Information about the *oxygen actually converted* in the organism can thus be obtained by measuring the CO_2 emission. The significance of this parameter is subject to three limitations, however:

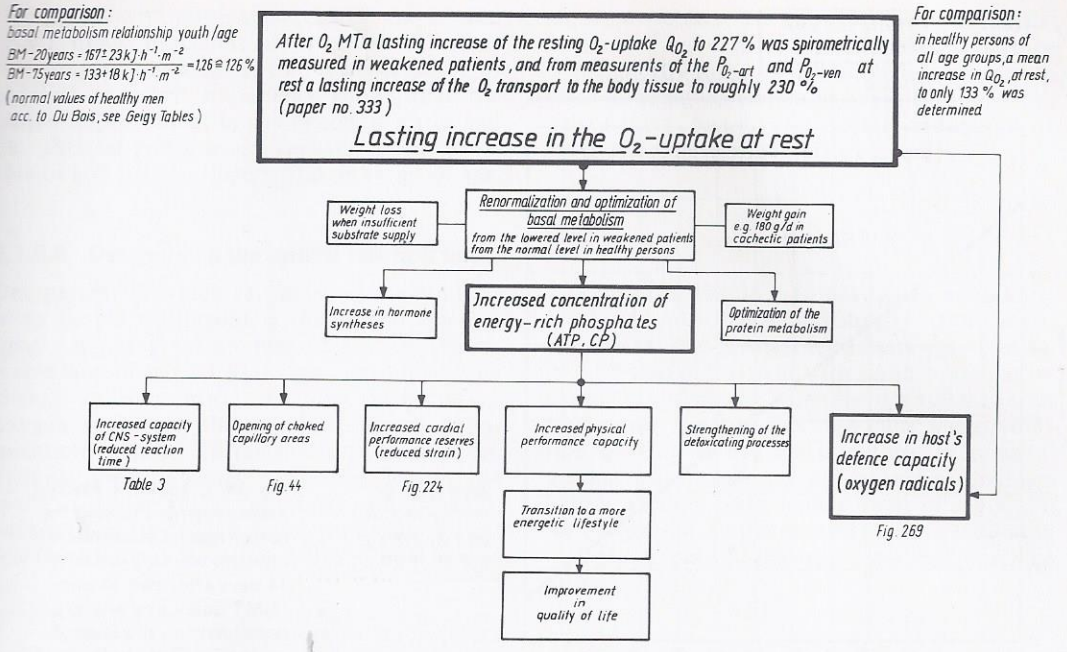

Fig. 23 Where in the organism does this extra absorbed oxygen remain? It follows from spirometric measurements (see appendix) that approx. 50% of the extra oxygen offered after O_2MT is metabolized to CO_2

(1) A not inconsiderable portion of the CO_2 formed is re-used immediately in the organism for syntheses (especially fatty acids), and therefore does not appear externally. It is important to know this for the basal metabolism.

(2) In comparison with a certain absorbed and used amount of O_2, the amount of the CO_2 formed per unit of time is also dependent on the type of nutrients as "fuel". Fatty acids contain less oxygen than glucose, for example; therefore the intensity of metabolism and CO_2 production is reduced at the same O_2 flow. These facts are reflected in the "*Respiratory Quotient*" (RQ):

$$RQ = \frac{CO_2 \text{ production } (ml \cdot min^{-1})}{O_2 \text{ uptake } (ml \cdot min^{-1})}$$

At standard conditions (basal metabolism the RQ is ~ 0.82, corresponding to a CO_2 production of 250 ml/min and an O_2 uptake of 300 ml/min. As a rule, RQ increases after O_2MT (e.g. up to 0.9) and with increasing performance. At about 2/3–3/4 of the maximum performance capacity (physical exertion) RQ reaches a value of 1.0, which corresponds to an exclusive glucose oxidation.

(3) In great *physical exertion* and corresponding metabolic acidosis (due to the anaerobically formed lactic acid) the RQ rises to over 1.0 as a result of an over-proportional CO_2 release with only a slightly or not at all increased O_2 uptake. The falling CO_2 partial pressure in the arterial blood indicates that the CO_2 expired comes from the normal blood stock and corresponds to a respiratory compensation (hyperventilation in maximal exertion) for the metabolic acidosis.

This excess CO_2 therefore does not stem from the oxidative metabolism, so that the CO_2 output measured under maximal exertion has only limited meaning.

1.1.5.8 Determining the physical performance capacity

Two series of experiments have been carried out to determine the physical working capacity (PWC) before and after O_2MT. In the first series (1982/83) we measured the PWC before and after *two 15 min O_2MT quick procedures* using bicycle ergometry with a gradual increase in load, and establishing the PWC_{130} (physical working capacity in watts at a pulse frequency

class sport, with implementation of the 15 min O_2MT quick procedure days or weeks before the competition. Singing, too, is a conversion of physical energies. Experience shows that the lasting improvement in the energetic status and the physical performance capacity seems to be able to give help to singers who, in terms of age, are approaching the peak of their vocal performance. An increase in the vocal performance (accoustically measurable), a longer preservation of the singing performance capacity during the culmination phase, and better endurance of extended appearances were observed.

1.1.5.9 Determining the optical reaction time

One parameter which can be easily determined using simple equipment is the *optical reaction time*[1]. Working on an idea of Fischer (Nordrach-Klausenbach, FRG) we examined the change in the optical reaction time due to oxygen multistep therapy [63]. Every determination is based on the mean value of 20 individual measurements performed within the space of 3 min. In 20 volunteers of both sexes, with a mean age of 60 years, the mean optical reaction time was reduced from 297 ms to 235 ms after the 36 h 15 day O_2MT procedure, i.e. by 44 ms or 16% (statistically significant at $p < 0.05$). The greatest reduction was observed in a 68-year-old patient with cerebrovascular insufficiency, from 515 (before) to 309 ms (after treatment). Thus in this case there was a reduction of 40% in the reaction time. In cases involving the existence of extreme tiredness before therapy, even higher levels of reduction were observed. In the control series, a reduction of only 5 ms or 2% was measured (training effect).

[1] For measurement of the critical fusion frequency and of the information flow to the short-term memory C_k see [62]

Table 3 Optical reaction time in milliseconds (ms) of 20 individuals before and after O_2 multistep therapy (mean values ± s.e.m. from 20 separate measurements each within 3 min)

No.	Sex		Age	Diagnosis	before O_2MT	after O_2MT	Difference	
	m	f	years		ms	ms	absolute ms	relative %
1		f	71	chronic CVI	275±42	260±52	-15	- 5,5
2	m		55	glaucoma	256±23	226±25	-30	-11,7
3	m		52	chronic IHD	245±46	204±27	-41	-16,7
4		f	55	migraine	292±96	215±27	-77	-26,4
5		f	52	glaucoma	295±56	298±82	+3	+ 1,0
6	m		76	ageing prophylaxis	209±56	199±17	-10	- 4,8
7	m		45	solvent exposition	202±18	185±23	-17	- 8,4
8	m		52	chronic CVI	253±76	231±33	-22	- 8,7
9	m		71	chronic CVI	282±82	258±46	-24	- 8,5
10		f	63	chronic CVI	276±46	218±21	-58	-21,0
11	m		68	chronic CVI chronic IHD	515±139	309±58	-206	-40,0
12	m		80	chronic heart failure	290±113	212±22	-78	-26,9
13	m		48	chronic CVI	295±141	224±22	-71	-24,1
14		f	63	chronic IHD	259±43	208±30	-51	-19,7
15	m		64	borderline hyperthyreosis	246±62	228±47	-18	- 7,3
16	m		57	chronic CVI	375±208	320±115	-55	-14,7
17	m		71	DAH	248±52	235±22	-13	- 5,2
18		f	40	chronic CVI	239±35	204±31	-35	-14,6
19		f	62	chronic CVI chronic IHD	302±64	256±26	-46	-15,2
20	m		55	diabetes mell. chronic IHD	228±27	220±30	- 8	- 3,5
20	13	7						
x±s			60,0±10,7		279,1±85,0	235,5±44,5	-43,6	-15,6

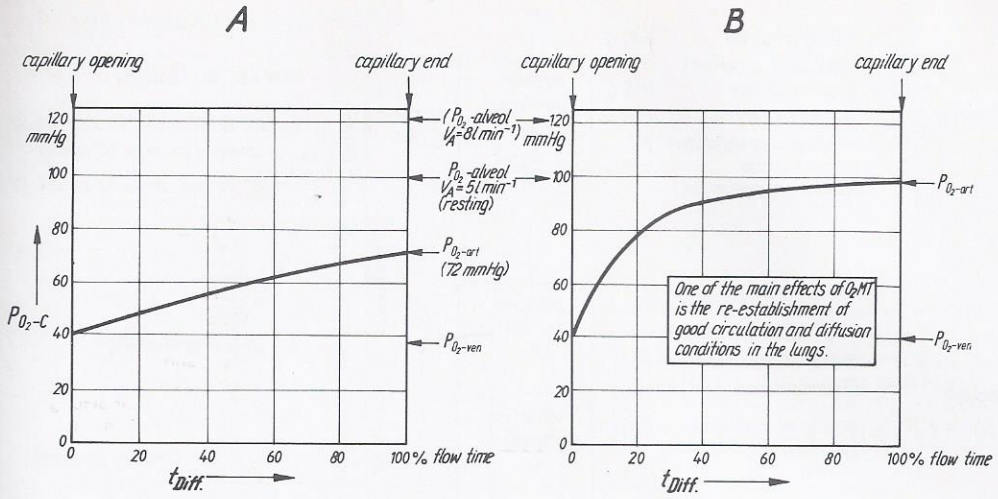

Fig. **28** Increase in O_2 partial pressure in the blood during the passage through the lung capillaries, represented for a 70-yr-old individual with reduced arterial resting P_{O_2} (A) as expected, and for a 70-yr-old individual with arterial resting P_{O_2} (B) lastingly raised by means of the O_2MT by 26 mmHg above the expected level, to 38 mmHg. 1 mmHg = $1.33 \cdot 10^2$ Pa

exertion brings about a great increase in the flow rate of red blood cells virtually saturated with O_2, despite the shortened contact time. The desired augmentation of the O_2 offer then occurs for the whole organism.

Just how much the O_2 saturation of the blood in the flow through the lung capillaries is worsened with the reduction in cardiopulmonal performance at an age of, e.g. 70 years, can be seen from diagram *A* in Fig. **28**. The course of the curve emphasizes to what extent the circulation and diffusion relationships in the lung belong to the target area of therapy, when we want to ameliorate or eliminate the reduction in cardiopulmonal performance with advancing age. Diagram *B* in Fig. **28** gives an example of the effects of the O_2MT procedure. It shows that the relationships in the lung system can often be regenerated, even in older age, to a degree previously hardly believed possible.

The interrelationships of the factors decisive for the $P_{O_{2\text{-art}}}$ and reactivity of the lung-heart system are shown in Fig. **29**. In particular, the couplings and feed-backs existing between the various elements have been drawn in here. The triggering factor of the reactivity can either lie predominantly in the lung or in the cardiovascular system, or together in both areas. The cellular switching mechanism of the microcirculation, which lastingly closes, or re-opens the capillaries in the diffusion-perfusion area of the lung, is primarily the main contributor to reactivity. Depending on the type of the triggering factor or of the regulatory mechanism, the reactivity has either a small (τ_1) or a large (τ_2) time constant. We must make a fundamental distinction between degenerating influences (−) which decrease the $P_{O_{2\text{-art}}}$, and regenerating influences (+) which increase the $P_{O_{2\text{-art}}}$.

Figure **30** shows a typical example of P_{O_2} reactivity with a small time constant. Another example of arterial P_{O_2} reactivity with a small time constant is the reduction of almost 10 mmHg (1.3 kPa) in the $P_{O_{2\text{-art}}}$ due to a dose of 1.6 mg nitroglycerol. Among others, Fig. **17** above is an example of arterial P_{O_2} reactivity with a large time constant.

1.1.8.2 The reduction in the $P_{O_{2\text{-art}}}$ due to age and stressful influences

In a non-selected group of patients the $P_{O_{2\text{-art}}}$ values vary over a wide range. Figure **31** gives information about the distribution of measured levels in patients at a physiotherapy clinic. There is a very pronounced and characteristic *dependence of the mean $P_{O_{2\text{-art}}}$ on age*, as can be seen in Fig. **32**. It is natural that the reduction in $P_{O_{2\text{-art}}}$ with age greatly contributes to

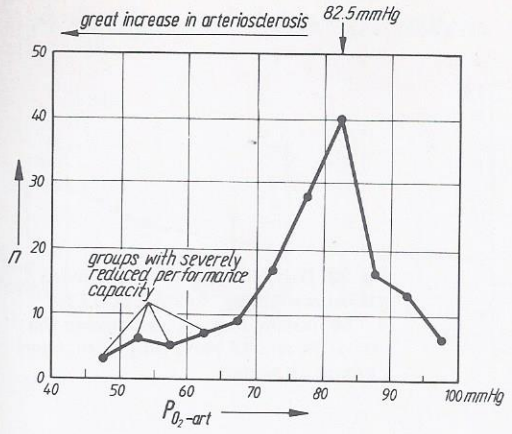

Fig. 31 Frequency distribution of the arterial P_{O_2} in clinical patients of all age groups (admitted under various diagnoses) acc. to measurements made by H. Krauss [84] on 150 persons under resting conditions. n = No. of persons with $P_{O_{2\text{-art}}}$ levels in the interval x ± 2.5 mmHg. 1 mmHg = $1.33 \cdot 10^2$ Pa

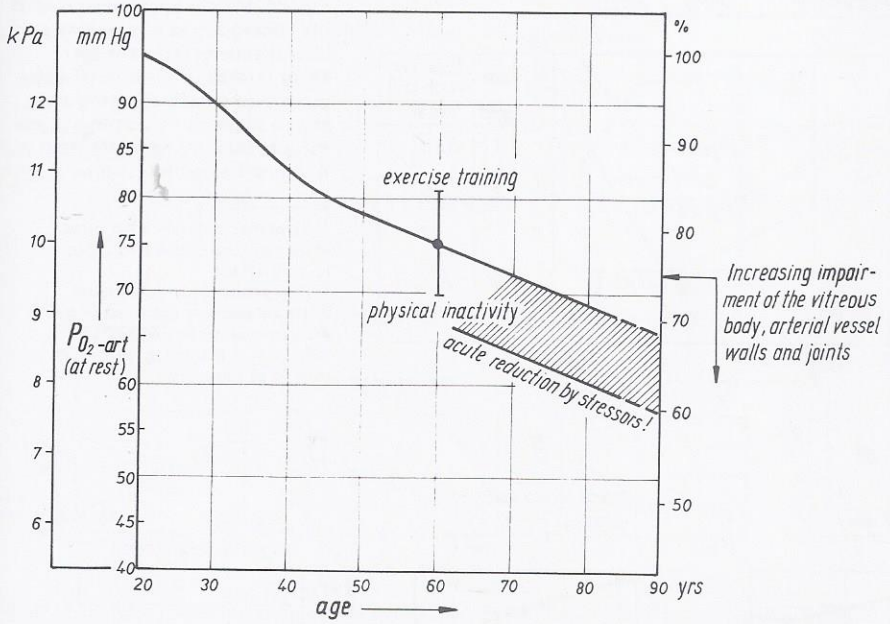

Fig. 32 Average dependence of the arterial oxygen partial pressure $P_{O_{2\text{-art}}}$, at rest, on age of healthy individuals from the working population, according to Loew and Thews [85]. The age-dependent decline of the resting $P_{O_{2\text{-art}}}$, which effects a relatively small reduction in the blood, particularly affects tissues that are supplied by direct arterial diffusion (Q_{O_2}). The resting $P_{O_{2\text{-art}}}$ is a characteristic for the ability of the lung system to take up oxygen (functional state, degeneration, regeneration)

the ageing of the human organism, in particular due to the decline in the arterial diffusion Q_{O_2}. Until our discovery in 1977 [3], this reduction was held to be a physiological regularity hanging over human life with fateful harshness. It was therefore very surprising for us and for others when experimental findings showed that it was usually possible, by means of an oxygen multistep procedure, to raise a reduced arterial P_{O_2} lastingly to levels which existed in the best years of youth.

The age dependency curve refers to mean values and healthy subjects. In reality, however, we must remember that levels very much lower than those in the curve occur temporarily when a minimum in the circadian cycle is superimposed on the $P_{O_{2\text{-art}}}$ minima caused by stressful influences (risk factors). Examples of $P_{O_{2\text{-art}}}$ changes within the circadian rhythm can be seen in Fig. 33.

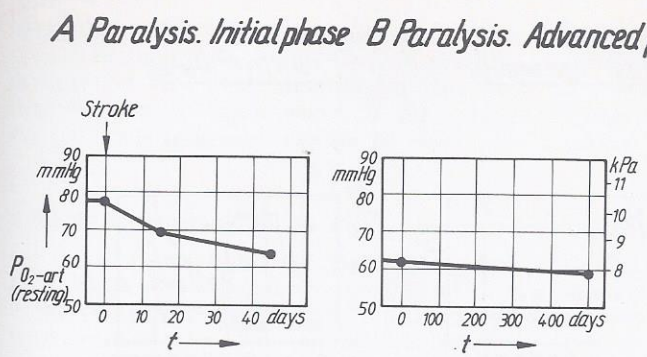

Fig. **36** Examples of the lowering of the arterial resting P_{O_2} by paralysis

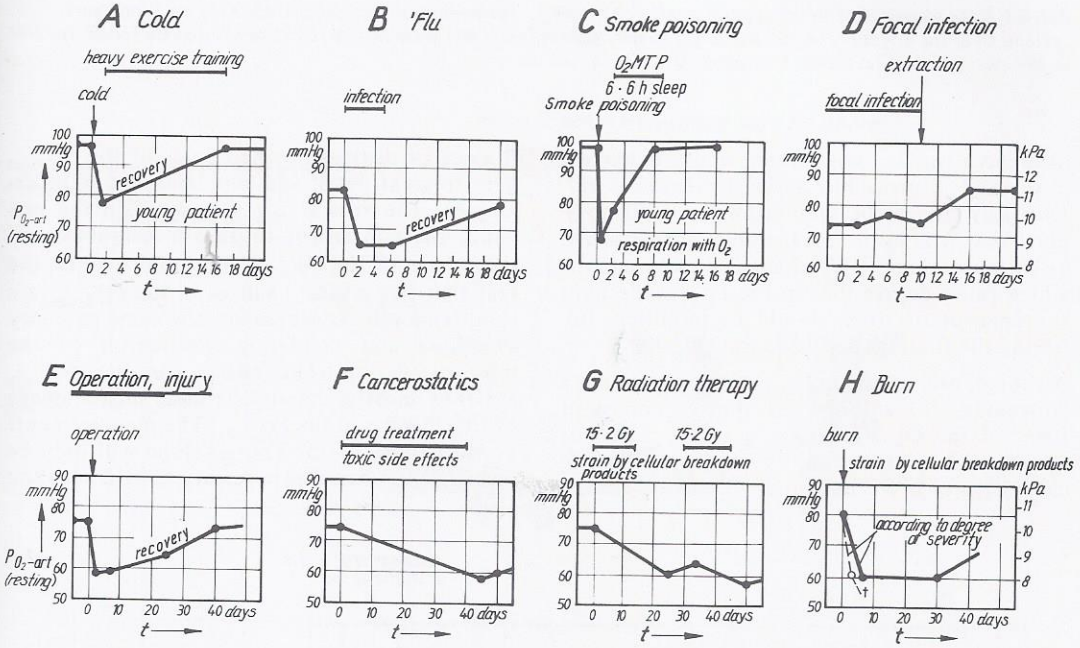

Fig. **37** Examples of the lowering of the arterial resting P_{O_2} by stressful processes of infectious, toxic, and quasi-toxic kind

lung-heart system reacts with a large time constant to most of the other stressful influences which we examined. It can therefore be assumed that the cellular vessel wall switching mechanism is decisive here.

One of the worst stressful influences of our time is the increasing lack of exercise in the modern lifestyle in industrialized states [87]. It is therefore no coincidence that *leisure sport in all its varieties* has become so widespread since the appearance in 1881 of Ferdinand Hartwich's pioneering, rousing work [88]. This development is a sign that a healthy instinct can lead people to do what is right, even when there are no measurements to prove its validity. Figures **35** and **36** give typical measurements showing the *reduction in the resting* $P_{O_{2\text{-art}}}$ *due to lack of exercise*. For the strength and temporal effect of further stressful influences, the cases compiled in Fig. **37** should be consulted. It can be concluded from examples *F* and *G* from this figure that, in the combat of cancer by means of cancerostatics or radiation therapy, the application of O_2MT is absolutely indicated as a protective measure to reverse the deterioration of the O_2 status, and thereby also to re-elevate the defence status. Examples in Fig. **38** show that the consequences of stressful

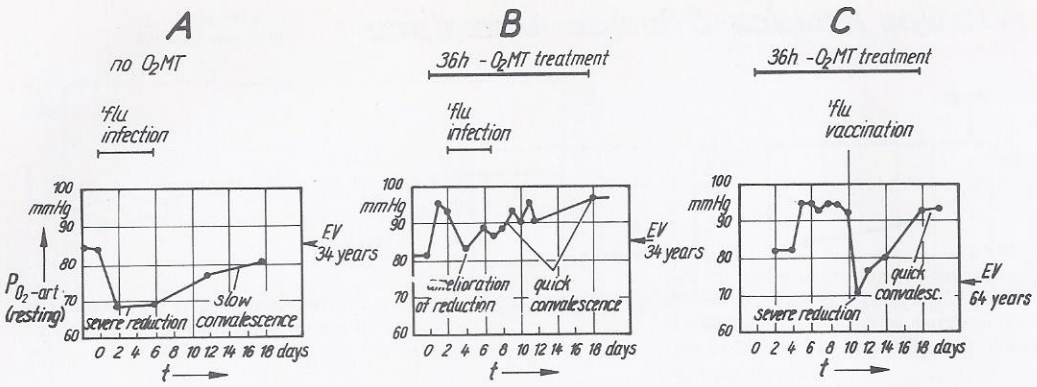

Fig. **38** Measurements of the change in arterial resting P_{O_2} (degeneration and regeneration of the lung heart-system) in a 'flu infection (A, B) and a 'flu vaccination without (A) and with (B, C) regeneration by means of O_2MT during infection phase. Examples. EV = expected value

influences can be ameliorated and combatted, if the O_2MT procedure is implemented *simultaneously*. It can be seen from the cases compiled that it is by no means only stressors such as those in Hans Selye's classical experiments, which cause depressions in the $P_{O_{2\text{-art}}}$. Perhaps the concept of stress should be modified, following the findings discussed in this book.

Although one of the consequences of stress is a worsening, for a longer or shorter period of time, of the O_2 status ($P_{O_{2\text{-art}}}$, $P_{O_{2\text{-ven}}}$, η), O_2 uptake, CO_2 production, physical performance capacity, etc.), we have only discussed the influence of distress on the course of the $P_{O_{2\text{-art}}}$ here in great detail and supplemented with examples. The reason for this was, on the one hand, the convenient routine measurability of the course of the $P_{O_{2\text{-art}}}$ and, on the other, the fact that the inverse changes in the $P_{O_{2\text{-ven}}}$ are simultaneously triggered by the same capillary switching and regulating mechanism of the microcirculation. The changes in the $P_{O_{2\text{-ven}}}$ are thus mostly the approximate mirror image of the changes in the $P_{O_{2\text{-art}}}$. The measurements of the course of the $P_{O_{2\text{-art}}}$ alone will only be insufficient when it is necessary to gain absolute

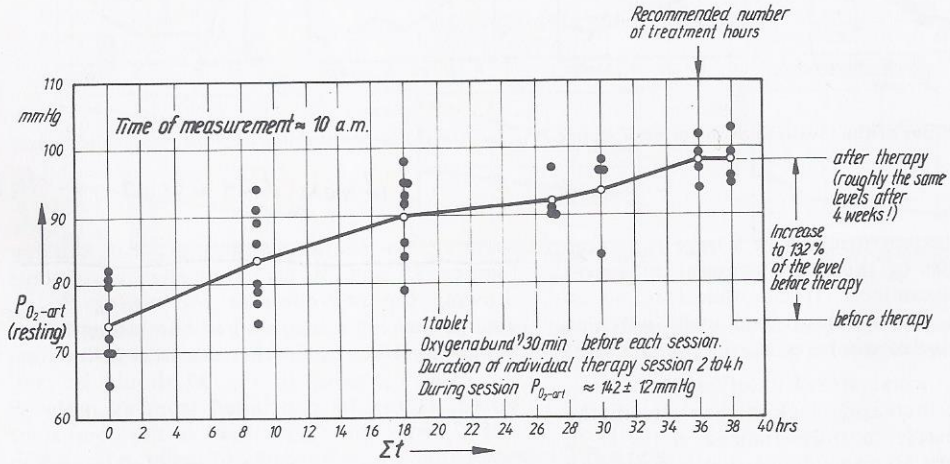

Fig. **39** Measurements of the arterial resting P_{O_2} as a function of the total no. of treatment hours ΣT of the O_2MT for healthy persons between the ages of 65 and 85 years. No of persons N = 8. Mean values. Daily exercise training. Result: lasting increase of arterial resting P_{O_2} to 132% of the level before treatment

[1] Containing 30 mg vitamin B_1, 50 mg Dipyridamol (Persantin), 100 mg Magnesium orotate

gered, which considerably contributes to the fast, large increase in η, i.e. to a great increase in the O_2 transport to the body tissue.

In the investigation into the contribution of the individual steps to the entire effect, one of the questions which we examined was that of the increase in η due to physical exertion. As a control in the program of the O_2MT quick procedure, O_2 application and drug administration were omitted in 3 further individuals. An increase in η, on average only slight and quickly declining, was then found (training effect). *The switching process of the microcirculation with its lasting effect was not triggered by 100 W physical exertion alone.* In contrast to the result in Fig. **44** right, an increase in the $P_{O_2\text{-art}}$ after strenous exercise training was generally also observed, if the strong physical exertion was repeated on several consecutive days. Figure **45** gives an example of this type. The threshold of the switching function can be crossed and a lasting P_{O_2} effect achieved, as documented by part "*d*" of the curve shown in Fig. **17**, by means of strong exercise training (daily 3 h gardening) over 1–2 weeks, e.g. mowing the lawn.

In older age and in the case of disease, the capacity for high-charging of η by means of stamina training or intensive sport alone is drastically reduced. Variants of the O_2MT, adapted to the individual performance capacity, are then to be chosen.

1.1.8.5 The level of $P_{O_2\text{-art}}$ and η, and its relation to the amount of circulatory reserves

In the discussion of our O_2MT research the following view has been repeatedly expressed by throroughly competent persons. It was said that the aimed for increase in the $P_{O_2\text{-art}}$ could bring about no improvement, as the gain in saturation attainable even in old age was only 4 %, and the reduced $P_{O_2\text{-art}}$ in old age was still sufficient to saturate the arterial blood almost completely with oxygen. This view is wrong for several reasons:

1. The gain of 4 % must be seen in relation to the fact that the arteriovenous exhaustion of the O_2 binding capacity of the blood is only 20 %. Hence, an increase of an additional 4 % in the O_2 transport means 1/5 more as compared to the original 20 %, and that is a great deal in stages of weakness.
2. The O_2 supply to the arterial walls, necessary for the maintenance of a good arterial vessel system (good O_2 supply to the tissue), occurs mainly due to O_2 diffusion from the lumen of the arteries and is therefore determined directly by the $P_{O_2\text{-art}}$.
3. The triggering of critical conditions, as was already pointed out above, does not generally occur when the arteriovenous saturation difference η on the HbO_2 dissociation curve corresponds to the expected value for that age under normal conditions, but when the value of η, particularly when near to the minimum in the circadian cycle, sinks far below the expected value, due to acute stressful events (e.g. infections, toxic stress, reduced cardiac performance, hypoxemia during sleep, high fever, chronic CO poisoning etc.). The more the mean level of the $P_{O_2\text{-art}}$ and η are raised, the greater the circulatory reserves and the smaller the probability that O_2 deficiency crises (e.g. dizziness, Ménière's disease, collapse, attacks of angina pectoris, myocardial infarction) will be triggered.

Figure **46**, especially, the patient examples on the left, gives a quantitative basis to the statement in the last paragraph. It is assumed in case *B* that the starting level of the resting $P_{O_2\text{-art}}$ is 72 mmHg (9.6 kPa), which roughly corresponds to the mean expected level for a 72-year-old. It follows from the further drawn scale of the HbO_2 saturation of the blood (standard conditions 37 °C, pH 7.4) that the degree of saturation is then still S_{O_2} = 93.3 %. As the further scale of the utilization of the O_2 binding capacity of the blood shows, this corresponds to η = 20.3 %, taking as a basis the normally applicable mixed $P_{O_2\text{-ven}}$ of 40 mmHg (5.3 kPa). The numerical values named, characterizing a circulatory condition which is still just about good enough, are drastically reduced when, as a consequence of stressful influences, a temporary drop in the $P_{O_2\text{-art}}$ and a rise in the $P_{O_2\text{-ven}}$ are triggered. The case *B* in our figure shows just how severely the numerical value of η, the $P_{O_2\text{-art}}$, and the O_2 saturation of the blood can deteriorate in such cases. The working points on the various scales shift to deep within the dangerous zone. The circulatory reserves converge towards zero.

A much more favourable situation exists in case *A* in Fig. **46**. When the starting level of the resting $P_{O_2\text{-art}}$ is high (between 95 and 100 mmHg ≙ 12.7–13.3 kPa), the O_2 saturation is almost 97 % and the exhaustion of the O_2 binding capacity of the blood approximately

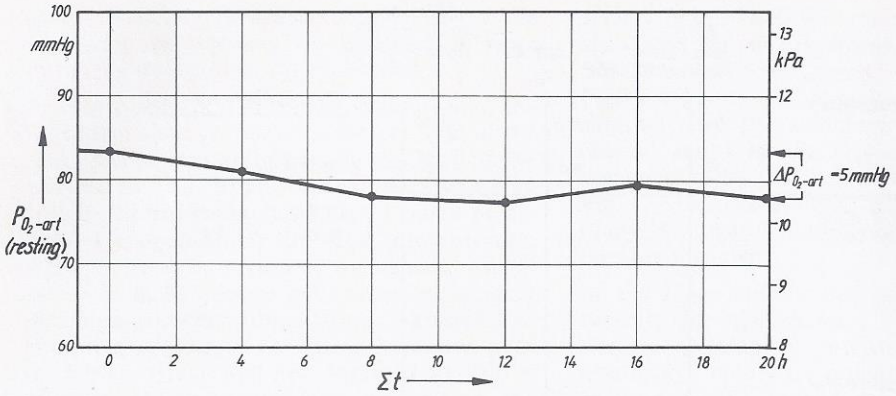

Fig. **47** Example of the behavior of the arterial resting P_{O_2} during the O_2MT treatment of real nonresponders (slowing of respiration by O_2 excess). Mean values of 3 patients [92]

The main indication for the O_2MT procedures should be seen as the *prevention of illness*. These procedures should always be used for prophylaxis at certain time intervals derived from P_{O_2} measurements, in cases of pathological movement disability or after approximately the 55th year of life (even earlier in exceptional cases of levels $P_{O_{2\text{-art}}} < 70$ mmHg ≙ 9.3 kPa). In youth and middle age daily strenous exercise training (leisure sport, jogging, running etc.) [12, 88, 95] is generally sufficient as a means of permanently increasing the value of η, or the $P_{O_{2\text{-art}}}$.

1.1.8.6 Lung-conditioned, O_2MT partial nonresponders; influencing factors, contra-indications

Like every other therapeutic procedure, the O_2MT also has contraindications and therapy nonresponders. There is usually a *contraindication* for patients in whom the body's respiratory regulation is not controlled as normal by the P_{CO_2} of the blood, but primarily by the low P_{O_2} of the blood (Loeschke's effect [96, 97]). In these patients the O_2MT can only be performed with special precautions[1].

In some patients, as Fig. **47** shows, even a reduction in the arterial resting P_{O_2} of roughly 5 mmHg due to the O_2MT procedure was observed. In these patients a drop in the $P_{O_{2\text{-ven}}}$ under O_2MT must have been attained.

As is known [96, 97], the arterial hypoxemia which exists in generalized respiratory insufficiency is associated with an O_2 deficient control of ventilation. Application of O_2 eliminates the adequate stimulus for the O_2 deficiency receptor, and so alveolar hypoventilation (with the reduction in the resting $P_{O_{2\text{-art}}}$ already mentioned), and also, in such cases, in increase in the $P_{CO_{2\text{-art}}}$ (hypercapnia) and the risk of apnea can occur. When the generalized respiratory insufficiency is considered to be a relative contraindication [98, 99], which is absolute under outpatient conditions, and when attention is carefully paid to the blood gas analysis and the acid-base balance in partial respiratory insufficiency, where we have never observed any dysfunctions, the O_2MT has proven its principal applicability under these circumstances, too. The temporary inhalation of oxygen in patients with chronic lung diseases and consecutive cor pulmonale has been successfully practised with the aim of reducing the resistance in the lesser circulation for years [100]. Whether, and to what extent, the O_2MT could have a comparable effect, is to be the subject of future investigations, appropriately in pulmologically oriented treatment centers. However, there can hardly be any risk for the patient in our therapy program with only a doubling or trebling of the O_2 content in the inhalation air in the 36 h procedure. The O_2MT, or the technology developed for it, can

[1] Artificial respiration if necessary. Recognition of patients with abnormal respiration regulation by means of initial test, e.g. with checking of the blood gases. For the dangers of artificial respiration for patients with severe chronic respiratory insufficiency using O_2 air mixtures with O_2 proportions > 50% (respiratory depression, arterial P_{CO_2} 60 mmHg, respiratory acidosis), see [98, 99].

the worse your lungs are the less O2 can be utilized

offer considerable help even to (particularly to) patients with severe chronic lung insufficiency (partial insufficiency).

The approach of crises is accompanied by a deviation from the normal acid-base status of the blood. For this reason we have always determined this status in the research phase in patients of this type. So far a change in status has never been observed in these checks.

The discovery in early 1982 of the drop in the resting $P_{O_2\text{-ven}}$ forced us to a *change in the assessment of responders and nonresponders to O_2MT*. True nonresponders can be defined as those individuals in whom there was neither an increase in the $P_{O_2\text{-art}}$, nor a drop in the $P_{O_2\text{-ven}}$, i.e. no improvement in the value of η due to O_2MT[1]. It is no longer permissible, as happened in [91], to class individuals in whom no increase in the resting $P_{O_2\text{-art}}$ is found, a priori as nonresponders to the O_2MT (see also Table **5** above).

Despite this fundamental finding, the question of the *influencing factors on the responder rate with reference to the increase in the $P_{O_2\text{-art}}$ is still of topical significance*, as the absolute value of the $P_{O_2\text{-art}}$ is in some important tissues of the organism (arterial vessel walls, lens of the eye etc.) alone decisive for the O_2 transport to the tissue, and good lung function alone benefits all the following links in the O_2 transport chain.

Indications of factors influencing the lung-conditioned, partial failure rate of the O_2MT were already be taken from a pilot study [92]. The study, carried out on 46 unselected patients (29 males and 17 females) within an age range of 34–75 years ($\bar{x}$ = 55.9 ± 11.3 years), with a total number of 20–30 treatment hours, showed that, with a mean $P_{O_2\text{-art}}$ under O_2 inhalation of 115.3 mmHg (≙ 15.36 kPa) instead of 125 mmHg (≙ 16.7 kPa), the failure rate rose from between 15 and 20% to 33%. It is certainly no coincidence that in the group with a high proportion of non-responders (failure rate 60%), a mean $P_{O_2\text{-art}}$ of 105.5 mmHg (≙ 14.1 kPa) was established during inhalation. It can be seen from these findings that the success rate in the application of the 36 h O_2MT procedure drops quickly when $P_{O_2\text{-art}}$ under inhalation remains below 125 mmHg (≙ 16.7 kPa) (oxygen flow too sparingly applied, e.g. < 3 l/min; particularly severe, advanced degeneration of the lung-heart system, e.g. chronic bronchitis).

According to the above, the measurement of the $P_{O_2\text{-art}}$ (20 min) after begin of O_2 application is one of the routine measures of the O_2MT. Examples of such measurements for the 36 h O_2MT procedure have been compiled in Figs **48** and **49**. In order to ensure that the threshold of the switching mechanism of the microcirculation will with great probability be crossed, the O_2 flow should be so adjusted that a $P_{O_2\text{-art}}$ between 125 and 145 mmHg (16.7–19.3 kPa) is measured under O_2 flow. This aim is often difficult to achieve, especially at the beginning of therapy (Fig. **49**). In such cases *all means should be used to increase the $P_{O_2\text{-art}}$ under O_2 inhalation during the first sessions.* The adjuvant means include: the increase of the O_2 flow to 5 l/min and more; activation of the applied O_2, HOT* procedure during O_2 inhalation; increase in blood fluidity; administration of 0.5 g nicotinic acid; drinking of a cup of strong coffee; treatment in a lying position with upper body at a lower level (resulting in a $P_{O_2\text{-art}}$ increase of up to 6 mmHg ≙ 1.33 kPa); preceding physiotherapy to improve respiratory technique [101, 102] and to improve ventilation values (gain of up to 15 mmHg ≙ 2 kPa); simplification of breathing training by means of the respiration biofeedback instrument [103] and, in chain smokers with CO poisoning of the hemoglobin of up to 20%, preceding detoxification by means of a 15 min O_2MT quick procedure [18].

According to the findings discussed, the group of *lung-conditioned partial therapy nonresponders* can be divided in six subgroups:

1. Structural pulmonary diseases with diffusion disorders, namely, in the existence of a generalized respiratory insufficiency. The proportion of such cases in nonselected patients is less than 10%.
2. Cerebrovascularly decompensated patients lacking compliance due to an organocerebral psychosyndrome.
3. Patients with a high proportion of shunt volume in the lung.
4. Individuals with severe CO poisoning (e.g. chain smokers).
5. Cardiopulmonally decompensated patients: a recompensation is a prerequisite here for the implementation of the procedure.
6. In persons with a high $P_{O_2\text{-art}}$ over 90 mmHg ≙ 12 kPa, e.g. due to physical stamina training), a higher level cannot be expected to be achieved.

[1] There is even a certain therapy success when the P_{O_2} levels remain the same, if a reduction in the cardiac output can be recognized (less strain on the heart)

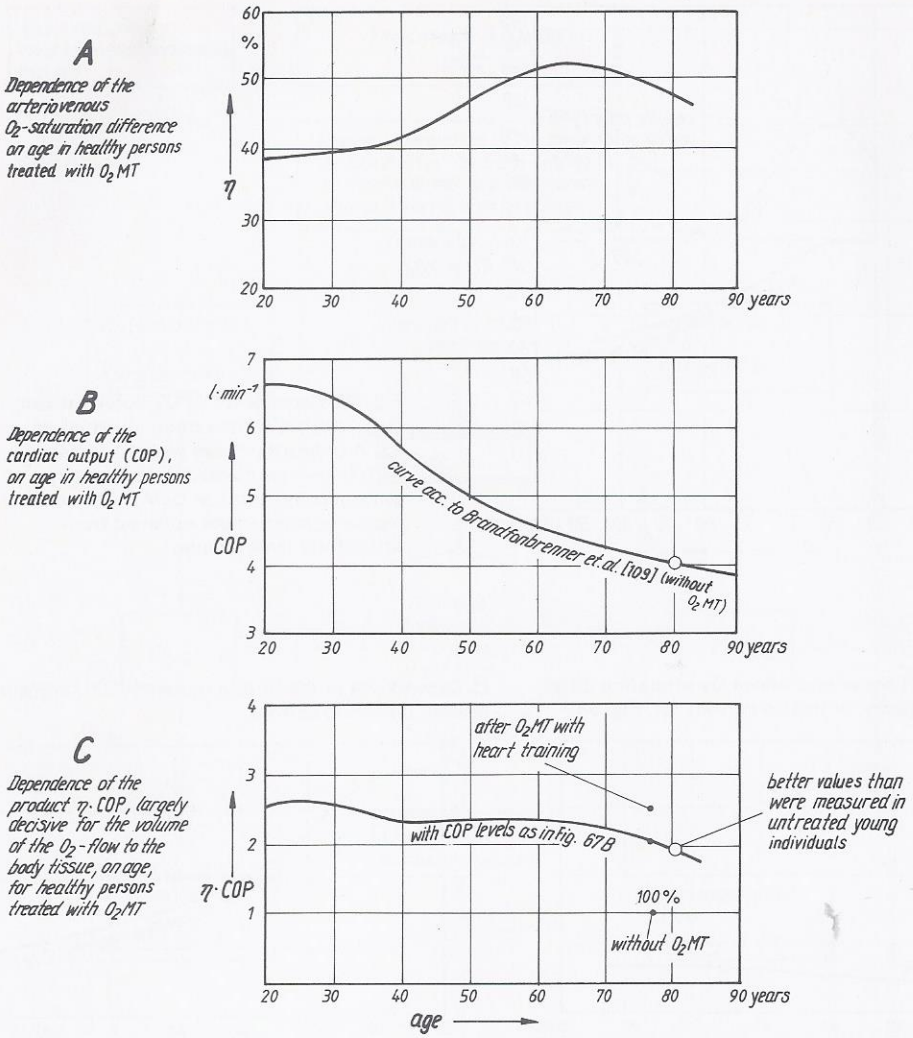

Fig. 68 The dependence of the arteriovenous saturation difference η (A), the cardiac output COP (B) and the product η·COP largely decisive for the O_2 flow to the body tissue, on age, for healthy persons after O_2MT. Mean value from a sufficiently large group of individuals. All values determined under resting conditions

where an improvement in the O_2 status is particularly desired. If the curve according to Fig. 67 B is used as a basis for the age dependence of the cardiac output, then the curve for the age dependence of the O_2 flow to the body tissue in accordance with Fig. 68 C is obtained.

From measurements of the CO_2 production (see Appendix), it follows that approximately 50 % of the O_2MT-borne, elevated O_2 offer are used for increasing the O_2 metabolism in the organism.

1.1.10 Differences in effects and indications between the 36 h O_2MT procedure and the 15 min O_2MT quick procedure

From the total overview of our findings so far (cf. also Tables 5 and 6) it can be seen that the effect of the 36 h O_2MT procedure lies somewhat more in the direction of an increase in $P_{O_2\text{-art}}$ (influence on the pulmonary function), and the effect of the single 15 min O_2MT quick

procedure somewhat more in the reduction of the $P_{O_{2\text{-ven}}}$ (influence on O_2 utilization). The quick procedure is particularly indicated in (younger) persons (subjected to severe distress) with $P_{O_{2\text{-ven}}}$ levels ≈ 40 mmHg. Furthermore, it seems that the increase in $P_{O_{2\text{-ven}}}$ as a consequence of distress is so pronounced that the lasting elevation in this value makes more frequent repetitions of the procedure necessary. The decision to undertake such repetitions can be much more easily taken with the quick procedure, as the *time* (also for the patient) *and oxygen required are only roughly 5% of that required for the 36 h O_2MT procedure*. The saving of oxygen is of great practical significance for all areas and countries where the O_2 provision from pressure cylinders or central facilities constitutes a bottleneck.

Due to the great savings in time and oxygen with the quick procedure, the question arises whether the 36 h procedure can be fully replaced by it. This question must be answered in the negative and not only due to the somewhat different effects discussed. The *36 h O_2MT procedure will be specifically indicated*, in the future also, *for patients with restricted mobility* (cardially or pulmonally limited performance capacity, diseases of the locomotor system such as coxarthrosis, gonarthrosis, peripheral circulatory disorders in the lower extremities, conditions after amputation of extremities, pronounced conditions of weakness, severe hypertension and other diseases being incompatible with the application of the quick procedure). The 36 h procedure with its supply of oxygen via the comfortable mask applicator will also be preferred in cases of respiratory insufficiencies (advanced lung emphysema, bronchial asthma, lung fibrosis, chronic bronchitis, conditions after pneumothorax), also in cases of limited psychic stress capacity (claustrophobia etc.).

The *15 min O_2MT quick procedure GK 2-I*, to be repeated once or twice, if necessary, *is indicated for sufficiently able-bodied persons* (elimination of acute conditions of weakness in younger and older persons, especially after operations, infectious diseases, accidents and other stressful events; further, to increase the physical performance capacity before stress of all types, like operations and particular physical strains, amelioration of jet-lag in journeys from east to west etc.). The use of the quick procedure has great possibilities in outpatient departments. For sufficiently able-bodied patients without much time, the 5 x 20 min O_2MT cure procedure GK 9-I (see Appendix) has been developed.

In extreme situations (e.g. severe circulatory disorders in the lower extremities, possible necessity of amputation) it can be recommended that the variants of the O_2MT be combined with the HOT* method, as has already been done (variant GK 4-III, [50, 74]).

1.2 Total irreversible blood microcirculation inhibition and capillary damage

1.2.1 Ideas about and investigations into the mechanism of the total capillary occlusion

It is, for the most part, the same elementary rheological mechanism which causes the *total, irreversible stoppage of the blood microcirculation and afterwards capillary damage*, in cardiac infarction, shock, inflammation and also in the modern concept of cancer multistep therapy (CMT). This mechanism is the continuation of the cellular capillary wall switching mechanism, representing the reversible phase and discussed in the previous chapters, to an irreversible end. The difference in the triggering of the mechanism consists mainly in the fact that the O_2 deficiency-conditioned endothelial swelling and the reduction of blood flow are accompanied by a considerable pH reduction; this pH drop is caused by a stronger or weaker transition to fermentation metabolism in the tissue surrounding the capillaries, and by the hampering of the drainage of the lactic acid formed. In this process pH levels of ≈ 6.6 can occur at the venous end of the capillaries, leading after a latent period to hemostasis.

This pH reduction causes a rearrangement in *the architecture of the biomembranes* [112]. This alteration in the membranes affects the microcirculation synergistically in many ways because, according to Table 7, changes occur, both in the blood cells and in the inner surface of the endothelium, which impede the microcirculation. Flexibility is critically reduced in

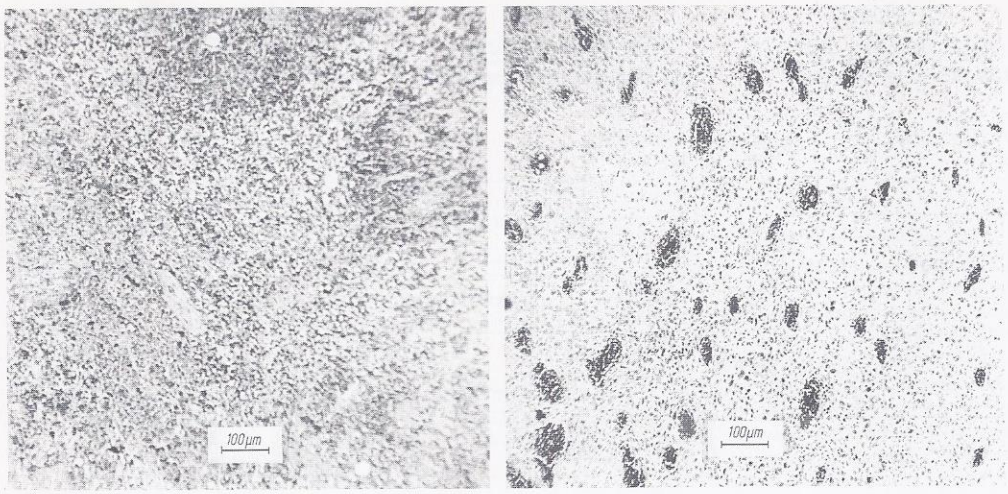

Fig. 74 Histological pictures showing the successful selective segregation of a cancer tissue (DS carcinosarcoma of rat) from the circulation through uniform triggering of irreversible hemostasis with the aid of extreme overacidification + 42.5 °C local hyperthermia and further measures of the cancer multistep therapy concept. The blood vessels are expanded and obstructed (B) (trichrome staining according to Goldner, green filter)

1.2.2 Cancer multistep therapy (CMT) and oxygen multistep therapy (O_2MT)

The central therapeutic mechanism in the CMT is the *selective irreversible closure of the vessels of the tumor* growing in the body [22, 23, 129]. This new method, used by us clinically with success for the first time in 1979, is fascinating for many reasons because:

1. due to the vascular obstruction, a segregation of the cancer tissue from the circulation of the organism occurs; thus the toxic strain on the circulation due to the sudden inundation by tumor degradation products is eliminated and at the same time the danger of internal bleeding is reduced.
2. the direct therapy target is not only formed by the cancer cells with their enormous variation in cell kinetic parameters, but additionally and mainly by the blood and vessel wall cells with their greater uniformity.
3. there exists justified hope that a universal therapy principle will be achieved, with individual arrangements in terms of tumor histology, vessel architecture, host tissue, stage and localization of the tumor, as all solid tumors are nourished via the blood vessels and must perish when these vessels are obstructed.

It is understandable that our ideas about the mechanism of capillary/post-capillary vascular occlusion have developed particularly from our CMT research. Figure 75 gives a summary of the new ideas developed in close co-operation with P.G. Reitnauer. We know today that both the formation of pores and the aggregation of red cells are favored by pH reduction. Compared with the course of the same mechanism in myocardiac infarction or inflammation [30] for example, the difference in CMT lies in the fact that the adjuvant step of local hyperthermia of 42–43 °C is necessary for the triggering of hemostasis, and to enable the contribution of endothelial swelling and red cell aggregation to become fully effective. This is obviously a specific characteristic of the cancer tissue capillaries (known to be previously dilated).

In our research to optimize the selective vascular occlusion, many series of experiments were carried out, partly also on the basis of suggestions kindly given to us by numerous colleagues. None of these efforts met with radical success. One idea presented itself at the beginning of 1982 from the O_2MT research, with the discovery of the bioenergetically controlled cellular wall switching mechanism, and from vital-microscopic investigations: there resulted, as a concrete measure to increase the probability of occlusion, the idea of *interrupting O_2 inhalation for a time at the start of the local or regional hyperthermia phase*, in order to promote, by a temporary drop in the O_2 offer,

1.2.3 Myocardial infarction and oxygen multistep therapy

As soon as a high percentage inhibition of the microcirculation occurs due to the mechanism of capillary/post-capillary blood vessel occlusion discussed (cf. Fig. 75), the drainage of lactic acid formed by fermentation is also hindered (hidden acidosis). This accumulation of lactic acid triggers a further feedback process, in the CMT procedure, in myocardial infarction and also in the late phase of shock with some temporal delay: the deceleration or stopping of the drainage of lactic acid leads to a gradual reduction in the pH at the venous and of the capillary from at first approximately 6.6 to 6.7 down to 6.0. Linked with this is an increase in the vascular leakage and red cell aggregation, and also a further loss in blood cell flexibility, i.e. an intensification of the occlusion. The time required for this pH reduction was determined at 150–200 min by in vivo pH recordings for CMT conditions. The time-span until steady-state overacidification is reached seems to be considerably shorter under infarction conditions (high-rate formation of acidic metabolites by the permanently working heart muscle).

This double feedback process explains the suddenness with which the infarction overcomes the victim. At the same time it can also be understood, however, that the infarction can be eliminated with the same suddenness in the initial phase of the acute ischemia, by a measure which increases the tissue pH. The portrayed *double feedback process in the triggering or interruption of the infarction* is a theoretically significant characteristic of the myocardial infarction which has hardly been discussed in cardiology as yet, perhaps because, although its pathogenetic rank in medicine was probable from observation, it is and can be seen in its functional context much more clearly by physiology and physics.

After the reduction of the pH in the myocardiac tissue concerned, there follows in the course of some 10 min the cellular release of lysosomal enzymes, which are activated with a factor of virtually 10 at pH values of around 6, and instigate the destruction of the relevant cells [141]. As soon as the outer cell membrane has been destroyed after about 100 min, the lysosomal enzymes which then enter the extracellular space contribute to the damage of neighboring cells, and the *lysosomal cytolytic chain reaction of the myocardiac infarction* [144], discussed below, proceeds after a further time delay of one to several hours, which in turn finally leads to the homogeneous large-area necrosis in the affected region of the heart muscle.

The answer to the *question of how long the course of the infarction mechanism remains reversible in the given temporal course* is of crucial practical significance for the design of a causal therapy for the initial phase of the acute myocardiac infarction. It is only possible in the reversible initial phase to bring the acute infarction to a halt by therapeutic measures. Measures which are not applied until later, in the irreversible phase, particularly in the clinic, can only spatially limit the self-maintaining mechanism, ameliorate it, and support the organism so that it can better survive, or survive at all, the time-span with reduced cardiac performance. In animal experiments we ascertained the amount of time up to the beginning of the irreversible tissue damage in the rat, by means of pH measurements in the rat heart, described below, under the conditions of a myocardiac infarction triggered by a coronary ligature. We found that the transition from the reversible to the irreversible phases occurs approximately 20 min after the infarction is triggered. If we use as a basis our estimation that pharmacologically therapeutic measures, with the aim of interrupting the infarction in its reversible phase, must be taken within 20 min, then it necessarily follows that *only the patient himself can undertake this primarily helpful measure*, as medical treatment is only in very rare cases available within 20 min of the infarction. It follows from this that only a therapy which has been prepared by the cardiologist in attendance (especially for high-risk patients), and which can be carried out by the patient himself, can restrict the triggering and spread of the infarction mechanism in an acute case. This conclusion practically forces us *to restrict these therapeutic measures to drugs with a fast and reliable effect when given orally or perlingually.*

One drug which fulfils this task supremely, as long as certain limits are observed in its dosage and application, is *g-strophanthin*. This drug, which was popular as a cardiac glycoside about 50 years ago, has nowadays been pushed well into the background, particularly by the slow-acting digitalis preparations. This is strange, because the very fast occurrence of the g-strophanthin effect (approximately 6 min after administration, compared with 90 min for digitoxin [145]) means that the ranges of indications partially overlap each other. Above all, however, therapeutic effects have been proven

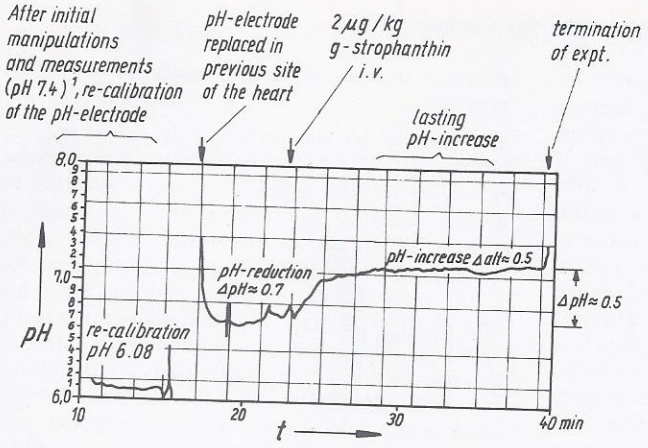

Fig. 84 The long-lasting, pH-increasing effect of g-strophanthin in the left ventricle of the myocardium [146]. pH changes during the early phase of an experimental cardiac infarction simulated by a controllable (clamping, lifting) ligature of a coronary vessel of the beating rat heart, and after i.v. injection of g-strophanthin. Part of an original strip-chart recording. pH measurements using a glass combination microelectrode

[1] Not shown here

for g-strophanthin, which have not been observed with digitoxin. Thus we found in accordance with Fig. 84 that the pH in the focus, which had fallen during an experimental infarction, rose again within 4 min of a dose of g-strophanthin [146]. The view, which can be found in old textbooks of cardiology, that g-strophanthin stimulates the degradation of formed lactic acid as an energy source of the heart muscle, can help us to interpret this. If g-strophanthin moderates in the initial phase the over-acidification which occurs in the focus, then the reversible formation of "pores" in the vessels and the stiffening of red cells and leucocytes must also be reduced, and the staunching of the microcirculation which has occurred must be more or less lifted. We have tested this conclusion with experiments. The confirmation of its correctness can be seen from the measurements summarized in Fig. 85. Photoelectronic measurements of the color index of the tissue with a micro-optical wave guide [121] did indeed show that the value in the focus greatly rises immediately after a dose of g-strophanthin (Fig. 85 A), that therefore the microcirculation is increased again [122], which leads to a favoring of lactate drainage and hence to a rise in pH. The mean oxygen partial pressure in the tissue was also simultaneously recorded in these experiments (Fig. 85 B). From this record it can be seen that, roughly at the same time as the increase in microcirculation caused by g-strophanthin, the mean P_{O_2} in the focus also increases considerably. It has thus been proven in animal experiments that g-strophanthin, applied early enough, can weaken the critical feedback process discussed, and restrict the infarction mechanism.

In attacks of angina pectoris, too, g-strophanthin causes, over and above the effect of the increase in pH, an increase in the microcirculation and thereby also in the O_2 supply in the area concerned. The result is, as a rule (in approximately 85% of cases [147]), an arrest of the angina pectoris attacks within 6–10 min of an ad hoc application.

A renaissance in the use of g-strophanthin can be expected following these findings if we can refute a claim which, despite experimental counter-findings, is unfortunately brought forward again and again: the incorrect claim that g-strophanthin cannot even be given perlingually with certainty of effect[1].

It follows from our investigation [150], in accordance with Fig. 86, that the strength of action of the oral/perlingual dose is largely dependent on the concentration of the solution applied. This means that the strength of action depends significantly on the accidental dilution of the glycoside with saliva, i.e. that considerable variations in the effect can be expected with this type of application. These variations can be avoided, however, and a high effect on the heart achieved, equivalent to the i.v. standard dose, if the dose (according to [15]) is applied perlingually in high concentration (e.g. from a Strodival special preparation, 6 mg = 6% in oleophilic phase). The administration is

[1] The idea that perlingually applied g-strophanthin is only slightly resorbed, and at a high degree of variation (Greeff, Verspohl) must be held to be incorrect, since it was shown in [148] that the applied g-strophanthin is found at its maximum concentration in the plasma only 24–48 h afterwards, and Erdle confirmed this result in his thesis [149]. According to [148], in this proportion of g-strophanthin released from the (tongue) tissue, we are only dealing with a residual molecule which is hardly toxic any more, and without glycoside effect

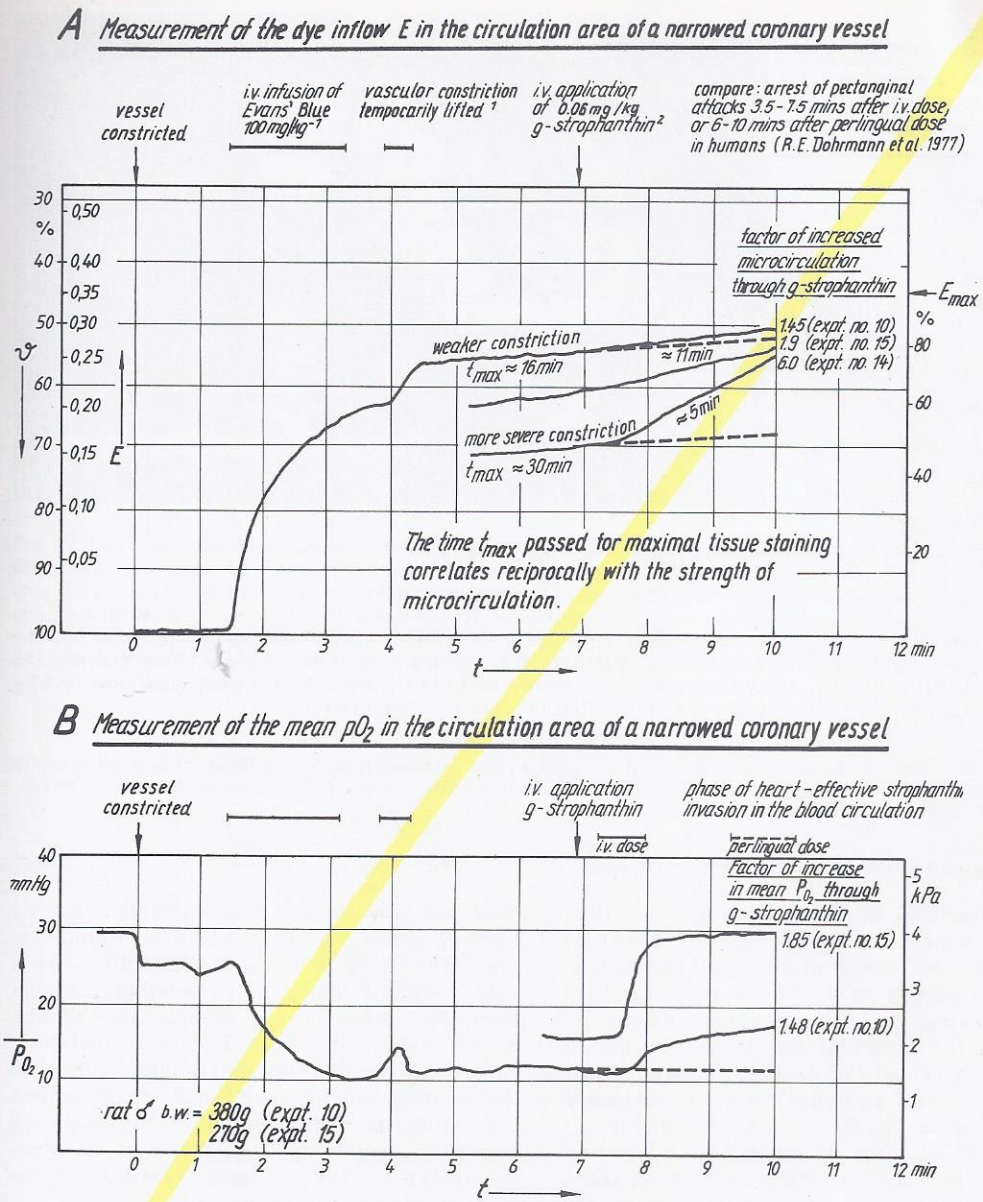

Fig. **85** Direct proof of restoration of microcirculation (A) and in the mean P_{O_2} (B) in the circulation area of a coronary vessel constricted to simulate cardiac infarction, immediately after application of g-strophanthin. Vital colorimetric measurement (A) using light-conducting micro-probe. Needle of light probe ground flat and attached on the tissue area of interest. ϑ = transparency, E = extinction

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1 Experimental control
2 Dosage adapted to species rat

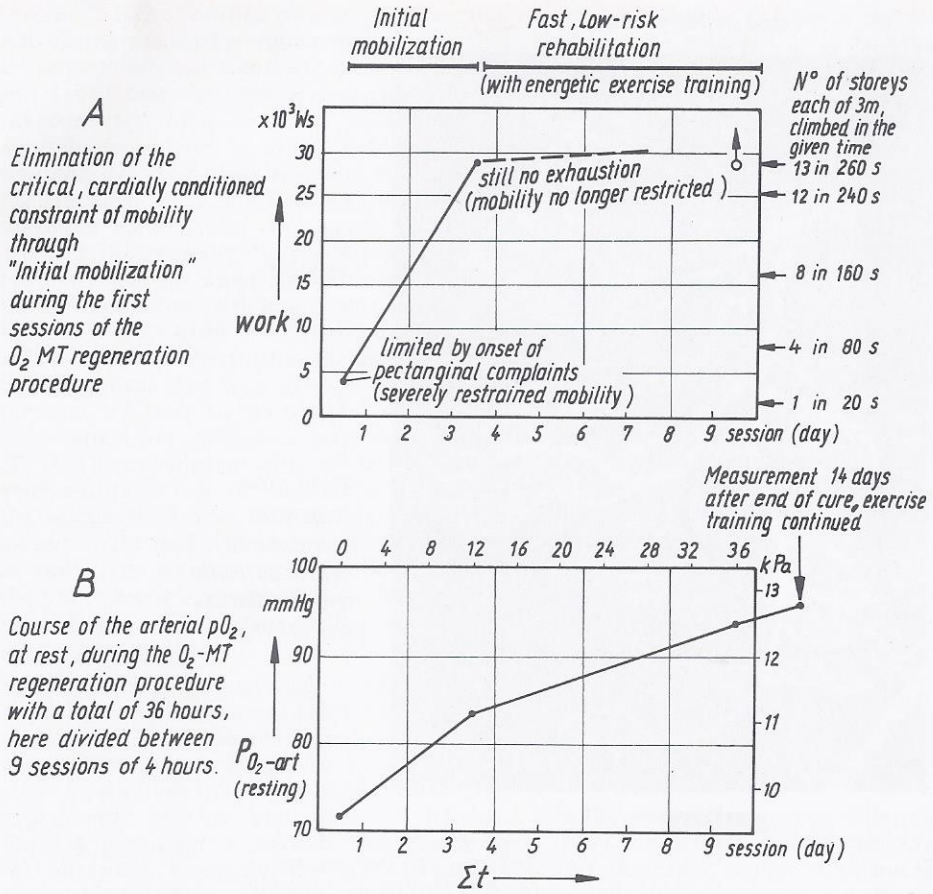


Fig. **89** Example of risk reduction and speeding-up of rehabilitation in a 55-yr-old infarct patient through initial elimination of cardially-conditioned constraint of mobility with the aid of the O_2MT procedure GK 4-I (A). This "initial mobilization" of the patient is of principal importance for the general problem of rehabilitation and is closely connected with the increase in the arterial resting-P_{O_2} (B) and the decrease in the venous resting P_{O_2} occurring during the O_2MT cure (increase of physical fitness)

1.2.4 Shock syndrome and oxygen multistep therapy

Shock is a clinical syndrome affecting ill persons with more or less acute onset of circulatory insufficiency; ill persons who are peculiarly dazed, sense increasing weakness, whose extremities are cold, and whose skin is cool and damp, who have a fast, weak pulse, in whom the excretion of urine decreases more and more, and in whom a drop in the arterial blood pressure can frequently – but not always – be measured. If the various causes which attack the different sites of the circulatory system are not eliminated in time – in other words, if the "point of no return" has been reached – than the causes and consequences of the acute circulatory insufficiency superimpose: the shock becomes irreversible. Shock needs time for its development and its clinical picture is determined by the juxtaposition of cause, host's compensation mechanism, and general and local consequences, which sometimes form a vicious circle. The purpose of the circulation is fulfilled in its periphery, that is, in the direct neighborhood of the respiring cells and tissues. In this respect, shock is a more or less acute failure of the circulation, in which locally and pronouncedly the capillary circulation drops acutely to below the requirements of the tissues, simultaneously in several organs. Thus the microcirculation becomes the key to the qualitatively and quantitatively controlled inter-

action between circulation and tissue. Hence the basis of all forms of shock is the common pathophysiological characteristic of the deceleration of the blood flow in the capillary network. The generally insufficient circulation in the periphery should be particularly considered here, especially the form which is triggered by O_2 deficiency from the most varied cause [158]. As with the selective vascular occlusion envisaged during the CMT, or with the mechanism of myocardiac infarction, there also exists a reversible and, subsequently, an irreversible phase in the largely analogous shock syndrome. We believe that it is not only the precapillary sphincters (hindrance of influx) and the postcapillary constriction (hindrance of outflow) [158], but also the bioenergetic control of the cellular capillary wall regulating or switching mechanism, discussed above, which play a role in the slowing down of the blood flow in shock. The therapeutic intervention in shock can only be successful in the reversible phase. The counter-measure which is consequently derived from the triggering cause is the *renormalization, as fast as possible, or, even more effective, the substantial improvement of the O_2 status in the reactive capillary endothelium*. In the usual treatment of shock events triggered by O_2 deficiency (hemodilution [47, 154]), the application of O_2, as early as possible, is a matter of course. The speed and extent of the improvement in O_2 status brought about by this measure can be easily determined by the measurement of the resting $P_{O_{2\text{-art}}}$ and $P_{O_{2\text{-ven}}}$ values. Due to the circulatory insufficiency, the lowered $P_{O_{2\text{-art}}}$ is often only moderately raised. It should be a principle that the facilities should always exist further to increase significantly the $P_{O_{2\text{-art}}}$ and the η-value by means of a combination procedure with simultaneous O_2 application and HOT*. We hope that the above comments will stimulate the implementation of pilot treatments with this combination procedure.

1.3 Oxygen supply to the tissue

1.3.1 General remarks on the limit of oxygen supply

The oxygen reaches the cells from the capillary blood by diffusion and is used by them in oxidative metabolism, whilst the carbon dioxide released as an end-product is simultaneously delivered to the capillary blood. The drop in P_{O_2}, or increase in P_{CO_2}, which thereby arises between the arterial and venous ends of the capillary, has already been indicated in Fig. 9. Since O_2 deficiency in the tissue limits the oxidative cell metabolism much sooner than insufficient CO_2 removal does, it is enough here to consider only the O_2 supply to the tissue.

The limits of O_2 supply (diffusion distance) which surround the capillaries at distances of some 10 μm, represent the *start of the zone of cell decay* in the living organism. They are of vital significance in the formation of the steady state between cell proliferation and cell decay in the intercapillary space of the tissue (organs). If these limits come too close to the capillaries, due to O_2 deficiency over a long period of time, then the cell decline triggered by this leads to a critical decrease in organ performances: *O_2 deficiency conditions or O_2 deficiency diseases* [159] occur. In special cases it is possible significantly to increase the O_2 supply by means of hemodilution or HOT* (improvement of the flow properties [47, 160]). The furthering of the O_2 supply limits is one task and an elementary process of the O_2MT.

1.3.2 Vascularization parameters and the O_2 metabolism characteristic as the boundary conditions for the O_2 diffusion field in the intercapillary space of the tissue

The basis of most of the pathological consequences of O_2 deficiency in the human organism is primarily the principles of the O_2 supply in the intercapillary space of the tissue. These principles can be theoretically and quantitatively formulated for idealized models with relative little mathematical-physical effort, provided the boundary conditions are known [161–163], and they are easily comprehensible.

application with a spatially very limited interruption in O_2 supply (the occlusion of certain blood vessels form an exception to this). When the oxygen supply is weakened, the extent to which the reaction mechanism discussed in the following sub-paragraphs are involved in the whole occurrence depends on the degree and duration of the reduction, the type of tissue affected, and other factors.

1.4.2 Energy gain by means of glycolysis in oxygen deficiency

The individual cell in the organism needs, for the maintenance of its structure and its readiness and ability to perform its function, a certain energy supply, which it mainly obtains from the *oxidative catabolism of nutrients*, when the O_2 offer is sufficient.

When the oxygen is lacking (anaerobic condition) the required energy can simply be gained by *glycolysis*. Under in vivo conditions the oxidative breakdown of 1 mol glucose delivers 689 kcal (2885 kJ) and is connected to the formation of 38 mol ATP. With 270–380 kcal (1130–1590 kJ) these represent the (physiologically) utilizable free energy which corresponds to an energy yield of between 39 and 55%. By comparison, the transformation of 1 mol glucose into 2 mol lactate is connected with a reaction energy of only 47 kcal (196 kJ), by which 2 mol ATP are formed. These correspond to only 16–20 kcal (67–84 kJ) and an energy yield of 3.4–4.3%. Thus the aerobic decomposition of glucose supplies a total amount of energy which is 15 times higher, and ATP which is 19 times higher, than glycolysis [175, 176]. It is therefore not surprising that the end-product of the glycolysis, lactic acid, still contains a high amount of energy.

Special relationships exist in the heart inasmuch as the heart muscle which is sufficiently supplied with oxygen, covers more than 50% of its energy requirements from the oxidation of fatty acids. Glucose contributes 18% to the energy gain, lactate 17%, pyruvate approximately 1% and ketone bodies 5% [177]. In conditions of hypoxia, however, the breakdown of fatty acids is reduced, and glucose uptake and breakdown increase, as does the breakdown of glycogen reserves; thus lactate thereby accumulates to a greater extent [178] and overacidification occurs. The joint use of the lactic acid as an energy substrate in the myocardium (and perhaps also in the brain with a contribution of glycolysis to metabolism of approximately 19%), can be strengthened by g-strophanthin [169, 179–182]. This effect is indicated by an increase in the pH in O_2-deficient areas of the myocardium, roughly 3 min after administration of g-strophanthin. This increase is found only with g-strophanthin, not with digitalis preparations. This confirms the old concepts (Sarre, Uhlenbruck 1953) that g-strophanthin, but not digitalis preparations, improves the O_2 supply to the heart muscle. It has been hardly considered that g-strophanthin (according to [148, 183], highly effective and with reproducible potency, even when applied perlingually), in addition to its main effect in the heart muscle, also triggers a peripheral effect. Due to its action on the vasculature, the blood flow is increased [185] and the O_2 and glucose supply is improved, particularly in tissue lying on the other side of the blood brain barrier [186, 187].

1.4.3 Target area in tissue for O_2 deficiency and O_2MT

The calculations of the dependence of the oxygen partial pressure P_{O_2} on the distance r to the capillary axis in the single-capillary model (Fig. **92**) referred to the P_{O_2} level (e.g. 45 mmHg) existing in the centre of the capillary. In reality the P_{O_2} drops, under normal conditions, from the arterial to the venous end of the capillary from 93 to 63–23 mmHg, depending on the organ (cf. Fig. **9**). For an example roughly corresponding to skeletal muscle, curve A in Fig. **97** shows the course of the P_{O_2} along the capillary, and curve B the course of the coaxial cylinder area of the distance r = 30 μm. The presentation shows that the *tissue area most at risk from O_2 deficiency is localized at the venous end of the capillary and at a great distance r from the capillary axis*. Under normal conditions the relative frequency is f < 2% for P_{O_2} < 3.5 mmHg (change to fermentation metabolism), and f < 0.2% for P_{O_2} < 1 mmHg (critical P_{O_2} of the mitochondria, irreversible cell damage), as can be roughly seen from the distribution curve in Fig. **98**.

The tissue area with high values of r at the venous end of the capillaries ("lethal corner") as discussed, forms, as can be seen in Fig. **99**,

then respired again, the drop in respiration rate due to the deficiency phase being only approximately 13%. The drop in the P_{O_2} level from 6.5 to 1 mmHg (0.87 to 0.13 kPa) is directly reflected in the record in Fig. **102** below. In the same figure above, the course of the pH in the bicarbonate-free Krebs-Ringer solution is recorded. The absolute values of respiration and fermentation of the myocardiac tissue are relatively low, evidently as a result of cell damage due to the manipulations undertaken. Despite this, the remaining metabolism suffices to allow us to see clearly in the solution, which is kept buffer-free, the time-point of the pH reduction due to the start of fermentation metabolism. It can be seen from the recordings in Fig. **102** that in the myocardiac tissue examined, the sudden change to fermentation metabolism occurs as soon as the P_{O_2} level in the solution sinks to below 3.5 mmHg (0.46 kPa). Roughly the same level is also found in other cell types. It can be deduced from the sudden transition to fermentation metabolism that even a relatively small improvement in the oxygen supply in the critical area of the tissue is usually enough to bring about respiration metabolism again, and thereby to eliminate the tissue over-acidification.

1.4.5 Over-acidification of the tissue

In order to become better acquainted with the over-acidification by glycolysis (caused by O_2 deficiency), we chose as a model the *myocardial tissue of the rat under simulation of a myocardial infarction*. The pH measurements were implemented by P.G. Reitnauer in the supply area of a coronary vessel, partially ligated, with a movable pH glass electrode on the beating rat heart [146].

Wistar rats placed on a thermostatically controlled stage under ethyl urethane anesthesia were tracheotomized, artificially respirated, thoracotomized and pericardiotomized. The exposed, strongly beating heart seemed at first to make measurement impossible, but was brought into a position as favorable as possible for the implementation of the ligature or measurement, by placing a nylon loop just a little way below the surface of the outermost apex of the heart. A thread under a left ventricular coronary branch was fed through the myocardium with a bent surgical needle, and made into a loose loop, in order to trigger later an experimental myocardial infarction. In order to throttle the large vascular trunks, the heart had to be turned upwards and the ligature positioned on its dorsal side. However, since it was difficult to manipulate the loop, now lying beneath the heart, during measurement, smaller vascular branches of the ventral side of the left ventricle were also ligated according to the individual shape of the coronaries. The "low-noise" pH measurement on the beating rat heart was made possible by very fine glass microelectrodes (Figs **103** and **104**) [190, 2], which had been developed in our Institute for measurements of the pH profiles of optimally over-acidified cancer micrometastases [189, 191, 2]. The largest diameter of the inserted part of such an electrode was only approximately 200 μm, so injuries critical to the heart function were avoided. A miniaturized (Pt/Ag/AgCl/0.9% NaCl in H_2O) unit served as reference electrode. For the measurement the reference and the indicator electrode were placed on the heart concentrically from both sides. After firm contact of the reference electrode with the surface of the heart, there followed the insertion of the tip of the pH electrode in the supply area of the coronary vessel branch prepared for the ligature, approximately 1 mm deep in the myocardium. The position of the heart was stabilized by the three points of contact, apex loop, reference and pH electrodes, enough to

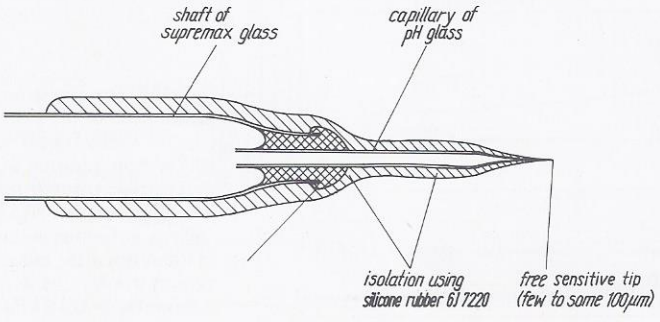


Fig. **103** Schematic cross-section of a pH micro-electrode

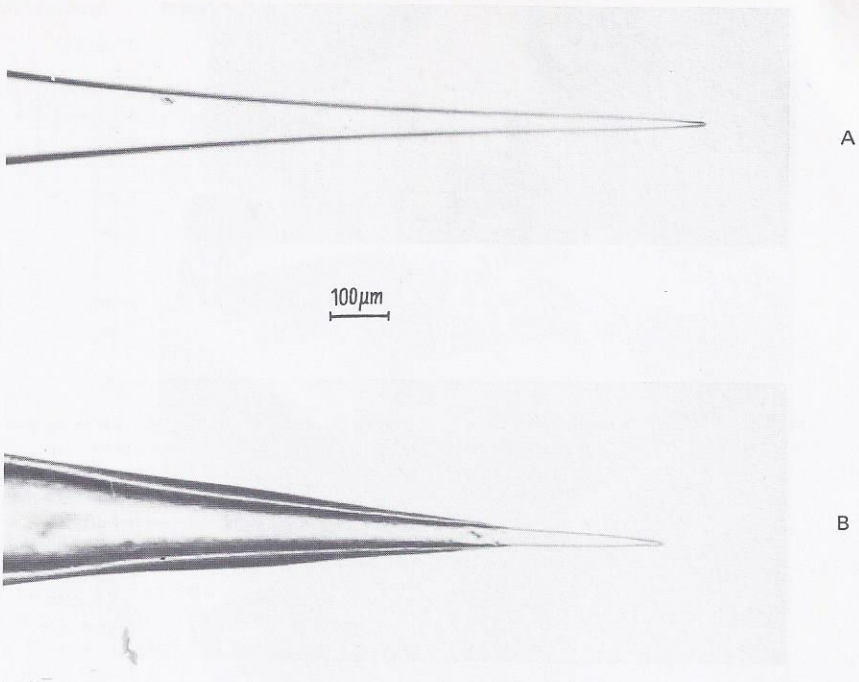


Fig. **104** Tip of a pH microelectrode before (A) and after (B) isolation with silicone rubber (free length of the sensitive tip is a few 100 µm)

make possible the measurement and recording of the pH values. Figure **105** shows this experiment in the stage before a small coronary vessel branch on the ventral side of the left ventricle was ligated. For the simulation of a coronary myocardial infarction, the loop used for this purpose could, after stabilization of the pH starting level, be more or less tightly pulled together using two pairs of tweezers and avoiding any further influence on the position of the heart; the loop could also, if necessary, be loosened again at a desired moment, by inserting a fine needle between the thread and the myocardium.

Using the experimental set-up discussed (Fig. **106**) we could *record the pH course in the O_2 deficient region of the myocardium of rats in the course of an experimentally generated infarction*. In all experiments there occurred a very substantial drop in the pH immediately after the triggering of the O_2 deficiency in the myocardium, as a result of a local increase in lactic acid concentration. It can be seen in Fig. **106** how the P_{O_2} in the supply area of the relevant vessel sinks by $\Delta pH = 1$ within 2 min, immediately after the constriction of a coronary vessel branch of the left ventricle. As a result of the incomplete ligature and a remaining supply from other sources (collateral vessels, diffusion from the environment), there occurs a pH level of 6.2. The remaining supply can be proven by the fact that, when artificial respiration of the animal is stopped, the pH immediately drops further and then reaches a level of 5.2 within 16 min. This also shows how fast and how low the pH in the myocardium must drop and cause damage to the tissue (microcirculation inhibition, vascular "porosity", increase in red cell aggregation, release and activation of the lysosomal enzymes, cytolytic chain reaction etc.) when, as can be expected in larger hearts (in humans for example), the infarct mechanism proceeds in such a way that there is no remaining supply from the environment.

The method of pH registration in a tissue area temporarily brought under O_2 deficiency is well suited to give information as to whether the damage caused by weakened supply (degree and duration of the impairment) is of a reversi-

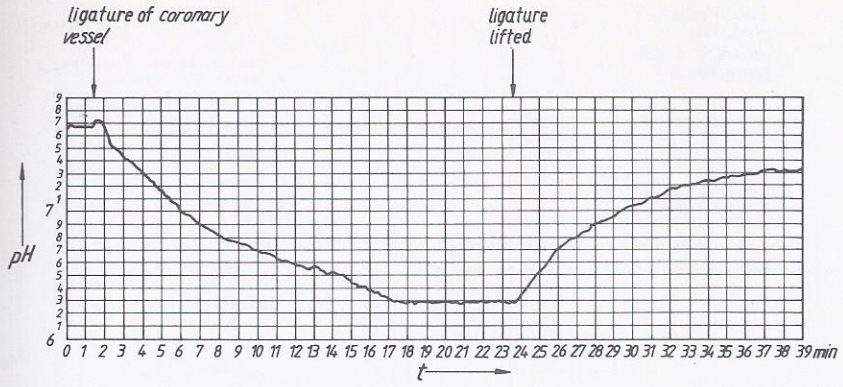


Fig. **107** pH course in the myocardium of the left ventricle of a rat, showing the reversibility of tissue impairment due to O_2 deficiency: pH renormalization after lifting the vascular occlusion as indicator. In another experiment of this type the blockade was not lifted after t = 24 min, but only after t = 50 min, and did not return to normal (irreversible tissue damage, stop in microcirculation)

ble or irreversible nature (cf. Fig. **95** above). Figure **107** shows an example of this. In this registration the pH drops from 7.7 to 6.3 after the vascular constriction, i.e. by 1.4 pH units, and quickly rises again to a normal level (7.3) after the vessel narrowing is lifted 22 min later. This shows how irreversible damage can be prevented and the metabolism of the tissue restored, by eliminating early enough the disturbance of supply. The *restoration of the pH in the affected tissue area after the removal of the disturbing factor can be regarded as an indicator of the still reversible nature of the damage.*

The duration of the phase in which the damage is still of a reversible nature (e.g. 25 min in myocardiac infarction) is, according to WHO statistics, only in 5% of all cases longer than the time until the start of emergency medical care. It necessarily follows from this that only the patient himself (informed, prepared and supplied with fast-acting drugs and, if necessary, also equipment) can aid himself effectively. *When risk factors exist, it is therefore one of the most pressing duties of the physician dealing with the case to equip the high-risk patient so that the danger of irreversible O_2 deficiency damage is minimized* (e.g. with the emergency package of "Strodival special", Fig. **87**, and, if necessary, also with 0.5 g methylprednisolone for risk of myocardial infarction, or with an oxygen carrier bag device for risk of stroke etc.). When irreversible damage has already occurred, the natural timepoint for particularly effective counter-measures has passed.

O_2 deficiency can have the most varied causes. One of these causes is an inadequate anesthetizing technique (intensity and duration). The measurement in Fig. **108** shows the fast, substantial drop in the pH in the cerebral cortex during the death of a rat, caused by an overdose of ether [2, 191]. We are dealing here with a very complex process, occurring in a larger confluent tissue area, a process in which not only O_2 deficiency in the nerve tissue, but also the *deficient situation* and thereby labilization of the blood-brain barrier [192], must play a role (see also Paragraph 1.4.10).

Connection between volume of the O_2-deficient tissue and amount of over-acidification. In the experiment in Figs **105** and **106** the volume of the O_2-deficient region in the myocardium is $V \approx 10\ mm^3$ (supply area of the narrowed coronary vessel) after 3–12 min. The pH drops to approximately 6.25. After t = 12 min, i.e. after termination of artificial respiration, the deficiency volume spreads over the whole heart, and a further steep drop in pH can be detected in the registration. This finding leads us to the question of the influence of the volume of the tissue affected by O_2 deficiency on the size of the pH reduction.

Because the lactic acid formed by fermentation is quickly drained off the cell, the intracellular pH of a single glycolyzing cell hardly drops below the level of the environment [191]. However, overacidification increases rapidly with increasing volume V of the cell conglomeration, as can be seen from measurements on micrometastases of different size [191]. The relationship between pH drop and volume of micrometastases consisting of almost 100% of glycolyzing tumor cells at a constant blood glucose level of $4 \cdot 10^{-3}$ g/ml is given by the

Table 11 List of sclerogenous noxae.[1] Disturbing factors which, according to W.H. Hauss, regularly trigger the unspecific mesenchyme reaction [172], detected by the increased rate of ^{35}S-sulfate incorporation into the sulfomucopolysaccharides of the ground substance of connective tissue in various organs (animal experiments)

Sclerogenous noxa	Disturbing factors
1 lack of oxygen[2]	hypobaric chamber with P_{O_2} values < 150 mmHg
2 hypotension	blood pressure amplitude too low (e.g. < 25 mmHg)
3 hypertension (Fig. 39)	reduced kidney circulation; hypertension (systol. blood pressure > 200 mmHg)
4 operations	anesthesia etc.
5 toxins	endotoxins, staphylococcus toxin, diphtheria toxin
6 infections	pasteurella multocida, staphylococci
7 nicotine	inhalation of cigarette smoke
8 foreign protein	albumin injection
9 allergic reactions	serum shock, Arthus' phenomenon
10 foreign substances	croton oil, plastic products
11 over-exertion	excessive movement in the treadmill
12 mechanical stress	laceration of muscle, dilatation of the aorta
13 interbrain stimulation	thalamus stimulation by means of electric current
14 emotional stimuli	binding, restricted movement
15 noise	roaring, uniform random noise
16 hormones	adrenaline, testosterone, thyroxine, cortisone, glucagon
17 influences of diet	sclerogenous diets

[1] Most of these noxae deteriorate the oxygen status
[2] Subnormal values of $P_{O_{2\text{-art}}}$ or η; locally reduced O_2 delivery to the vessel wall; mechanical irritation at ramifications in the arterial system

sclerogenous irritation or O_2 deficiency lasts for a long time (reduced clearance capacity due to energy deficiency) and particularly if such long-lasting conditions frequently recur, then the non-decomposable deposition products from the metabolism (collagen fibre bundles, calcification etc.) accumulate in the way shown by the electron micrographs in [172]. The damage to the vessel wall caused by these breakdown products no longer recedes (irreversible phase), as the increase of the diffusion length in both directions of the vessel wall (radial, central) begins definitively to limit the metabolism there. A final stabilization of the hypertrophic structure thus occurs. We therefore believe that the pathological changes in structure of the vessel wall remain reversible for a long time. The important thing is that the arteriosclerosis be combatted in this phase, before the irreversible wall degeneration finally takes place. We have already seen [2, 8, 106] the reversal of the sclerogenous noxa "oxygen deficiency" as a *method of renormalization of the vessel wall structure in the reversible phase*, i.e. the O_2MT in a highly intensive variant adapted to the part of the body in question.

Strict fasting discussed in Paragraph 5.3.9 (Table 42) should also be mentioned as a further method for the renormalization of arteriosclerotically degenerated walls of arteries and arterioles, and of degenerated layers of the alveocapillary system of the lung.

According to [172] the pathological changes in the vessel wall structure caused by the non-specific mesenchyme reaction affect mainly arterial vessels and their ramifications. Despite this, this reaction could always result in a deterioration of the O_2 supply to the tissue via capillaries, above a certain intensity. This deterioration should result from the reduction of the blood flow (cross-section narrowing, reduction in vasomotoric adaptability and in the air chamber effect) in sclerotically degenerated arteries.

A related reaction in the fine blood capillaries causes the vessel wall thickening discussed in 1.1.1, and thereby a narrowing of the lumen and even a direct hampering of oxygen and substrate diffusion to the intercapillary space. The *basal membrane thickening of the capillaries* due to protein deposits is a well-known phenomenon in diabetic (micro)angiopathies and kidney diseases. The same process can also occur in the membranes of the myelin sheath (Paragraph 1.4.11) and then leads to the neuropathies of the diabetics. In connection with this we should mention that these pathogenic basal membrane thickenings can be broken down by strict fasting (and also by O_2MT).

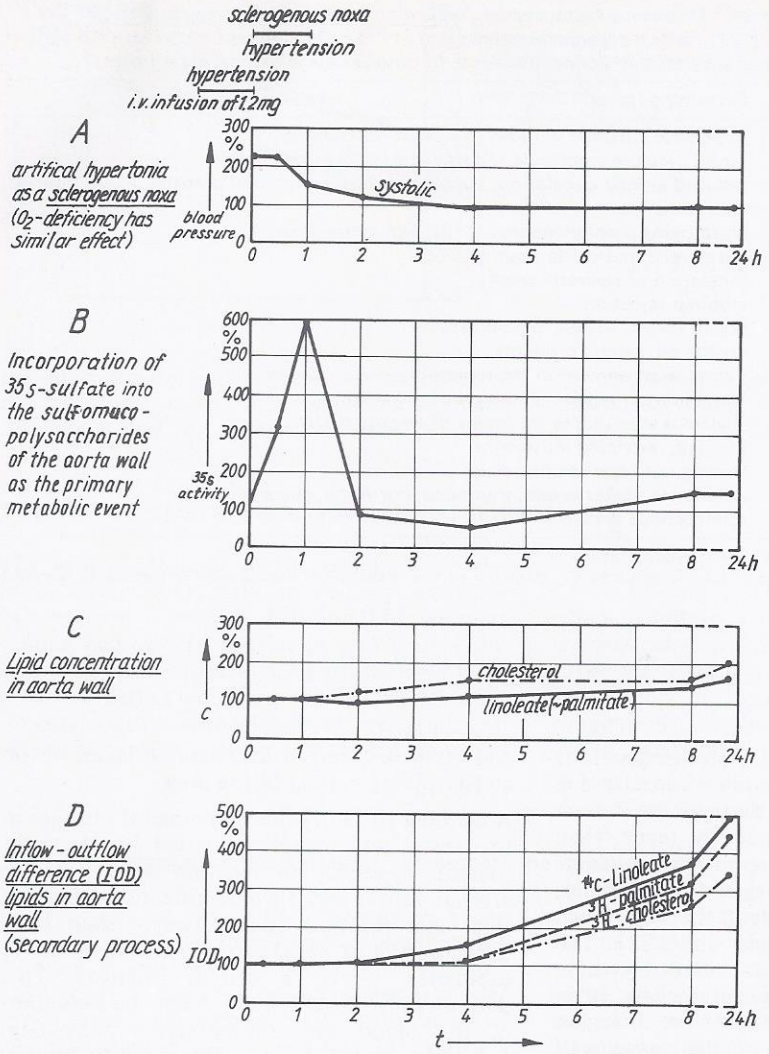


Fig. **113** Measurement on rats to show the fast onset of the unspecific mesenchyme reaction (B) after the raising of a sclerogenous noxa (A). The deposition of lipids into the vessel wall only occurs about 6 hours after the incorporation of mesenchyme (C) (D). Modified according to [172]

[1] A related fast reaction might be the swelling of endothelial cells in capillaries, likewise triggered through O_2 deficiency

1.4.8 Triggering of the formation of lysosomes

The *lysosomes* discovered by De Duve are membrane-delimited cell organelles which fulfil various functions. The primary lysosomes, formed from the endoplasmatic reticulum and the Golgi apparatus, contain in a "packaged" form (with great stability against their aggressive contents) a mixture of more than 35 enzymes, mostly hydrolases [195], whose activity optimum generally lies in the acidic range (pH = 5–6). The enzyme mixture is composed in such a way that it fulfils the following *main functions*:

1. Autolysis of the cell as soon as, on their death, the lysosomal membrane breaks off and the enzymes are intracellularly released;

2. Basis of the main therapy steps

2.1 Increase in the O_2 content of the inhalation air (2nd step) Ways lastingly to improve the utilization coefficient η of the O_2-binding capacity of the blood

2.1.1 Reduction in cardiopulmonal performance with age

One physiological "rule" that hung over every human life until 1977 is the *severe reduction in lung performance or in cardiopulmonal performance of the adult organism with advancing age*, portrayed in Fig. **123**. This rule should always have been placed at the beginning of all textbooks on geriatrics. The knowledge of this "rule", which was discussed in detail in 1.1.9.5, led us around 1970 to the question as to whether this drop in performance can be temporarily compensated or delayed using the means of today's science and technology. Much of the contents of this book emerged from the efforts to gain a positive answer to this question.

The above thought arose after we had in 1969 used oxygen for circulation support in whole body hyperthermia with core temperatures of up to 41 °C, with good results [2, 218]. At that time the author had the idea that, in order to balance the age-conditioned drop in cardio-

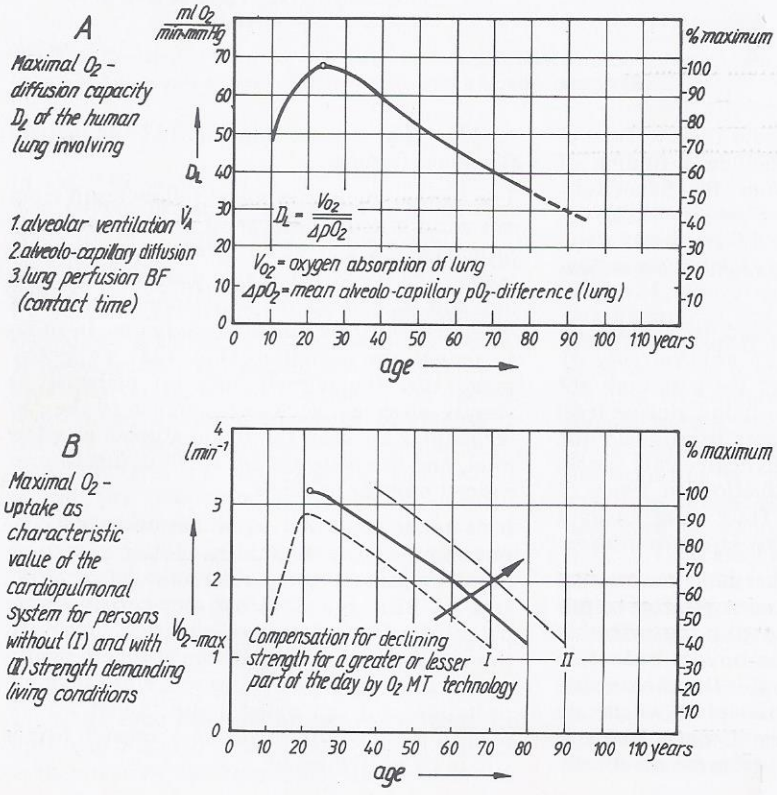


Fig. **123** Maximal O_2 diffusion capacity of the human lung (A) [216], and capacity of the cardiopulmonal system (B) [217] as function of age. In B, the age-dependent decrease of HMV, described in Fig. **67B**, is considered

[1] Environmental conditions of a modern industrialized state

[2] Favorable constitution, acquired in particular through exercise training

pulmonal performance (see also [219, 220])[1], technology would have to be developed which would allow a daily O_2 application with an O_2 flow of 2–4 l/min over the 24-h cycle (but at least for 8–10 h) with only moderate expenditure of means. Therefore the development of processes and instruments with the production of oxygen from air or water was begun in our Institute at that time. The result was the "O_2 Selector" described below (modern version manufactured by Hauniwerke, Hamburg, FRG). We know today that such equipment used permanently 24 h per day, e.g. in severe chronically obstructive lung diseases, can increase life expectancy by approximately 7 years [100]. However, we surprisingly discovered [3, 7] that, *even without permanent O_2 application*, the reduced cardiopulmonal performance in old age can often be increased for months up to years to levels existing in youth, if, by means of the three main steps of the O_2MT, the cellular capillary wall switching mechanism described in 1.1.1 has been triggered in the whole body and has led to the lasting distension of all capillaries.

2.1.2 Various ways lastingly to (re-)increase the utilization coefficient η of the O_2-binding capacity of the blood by O_2MT and exercise training

In order to maintain the increase in the O_2 offer to the body tissue or in the resting O_2 uptake, which endure for a long time after the end of the treatment and which represent the characteristic of the O_2MT, it is necessary to trigger the cellular capillary wall switching mechanism of the microcirculation in a positive direction (detumescence of the endothelium). This "steering' is possible by means of various combinations of measures, all of which we want to summarize under the concept of procedural variants of the O_2MT. Common to all the procedures is that they raise the energy or O_2 supply situation above a certain threshold for a certain time. If this threshold is crossed for a certain length of time, then the improvement which occurs in the microcirculation is maintained for a long time.

Typical dosage characteristics of the procedures for the high-charging of the blood microcirculation are compiled in Table 1. The *P_{O_2} level at the site of the endothelial cells at the venous end of the capillaries* (cf. Figs 3 and 7), *and the circulation volume of the microcirculation* are decisive for the triggering of the switching process. The higher the quantitative values of these parameters, the shorter the treatment time required. A procedure duration of roughly 36 h is necessary in order to attain the O_2MT target, so long as the physical exertion normally obligatory for the O_2MT cannot be performed (non-able-bodied patients) or is carried out between the treatment sessions and the O_2 content in the inhalation mixture is only approximately twice that of the normal level of the air, and so long as the normal respiratory minute volume (RMV) is only between 4 (sleeping) and 7 l/min (at rest). If, however, physical exertion of, e.g. 50–100 watt (home trainer) is performed during O_2MT treatment, the RMV rises to levels of between 20 and 33 l/min, and if the volume of inhalation of virtually pure oxygen is aligned with this significantly increased RMV, then P_{O_2} levels of an average 60 mmHg (8 kPa) result at the venous capillary end. Since the circulation of the capillaries in the lung and heart area is increased by a factor of approximately 2.3 simultaneously with the increase in cardiac output, a procedure duration of 15 min is then sufficient for the intensification of the microcirculation. The possibility of combining the two procedures just mentioned in O_2MT variants, and ways of designing such variants whose procedure duration lies between 36 h and 15 min, are discussed at a different point in this book.

The findings in [50] show that the method of so-called *hematogeneous oxidation therapy* (HOT* method, ultraviolet irradiation, UVI) according to Wehrli [222], also often intensifies the microcirculation. But this effect frequently fades in the course of a few days, because the efficacy of this method obviously remains close below the switching threshold discussed above (cf. Table 1). Our experiences indicate that the switching effect of the HOT* varies for the different tissue areas of the organism (good effect at the lower extremities). In order to extend the probability of a longer lasting effect for the HOT*, we introduced its combination with procedural variants of the O_2MT [50].

The risk to the patient is minimal in the HOT* method, which works without blood foaming [223]. The risk is higher in the invasive application of ozone [224, 225]. The same catalytic

[1] Mean levels of changes in 21 further physiological parameters between the age of 20 and 65 (normal conditions) are compiled in [221]

action of oxygen radicals is to be assumed, and the same limitations and features as with the HOT* should apply. The actual mechanism of the radicals, formed by short-wave UV radiation, by ozone and also by O_2 activation, as regards the reduction of the endothelial swelling, and the increase in blood fluidity [262], is as yet unexplained. However, what matters is not the explanation, but the effect (which can even be measured here).

Observations made at the capillary wall in diabetic microangiopathy have a certain connection with the reversal of the endothelial swelling of the capillaries dealt with here. In that case, too, a thickening of the capillary wall occurs, which is, however, attributed to an increase in the thickness of the basal membrane of the capillaries [229–233]. It has not yet been investigated whether this type of thickening can also be reduced by O_2MT procedures.

2.1.3 P_{O_2} increase in the inhalation air in high fever and in hyperthermia. Reduction of the rehabilitation time

In high fever, or with high artificial whole body hyperthermia, the O_2 binding curve of the blood is shifted towards the right in its upper part, as seen in Fig. **124**. For $P_{O_{2\text{-art}}}$ = 70 mmHg the O_2 saturation drops by 5.5 % from S_{O_2} = 93 % to 87.5 %, when the body core temperature has risen to, e.g. 42 °C. Figure **125** shows an *example of the change in the relative characteristic value of the O_2 status* ($P_{O_{2\text{-art}}}$, $P_{O_{2\text{-art}}}$, η, each at rest) *in a flu infection with 40 °C fever* (patient 30 yrs old). The discovered great increase in the resting $P_{O_{2\text{-ven}}}$ makes the main contribution to the critical reduction of the η-value to 13 %. Roughly the same low levels of η were observed in phases with substantial energy deficit. They are a characteristic *feature of conditions of weakness*. In such conditions even slight dysfunctions in the cardio-

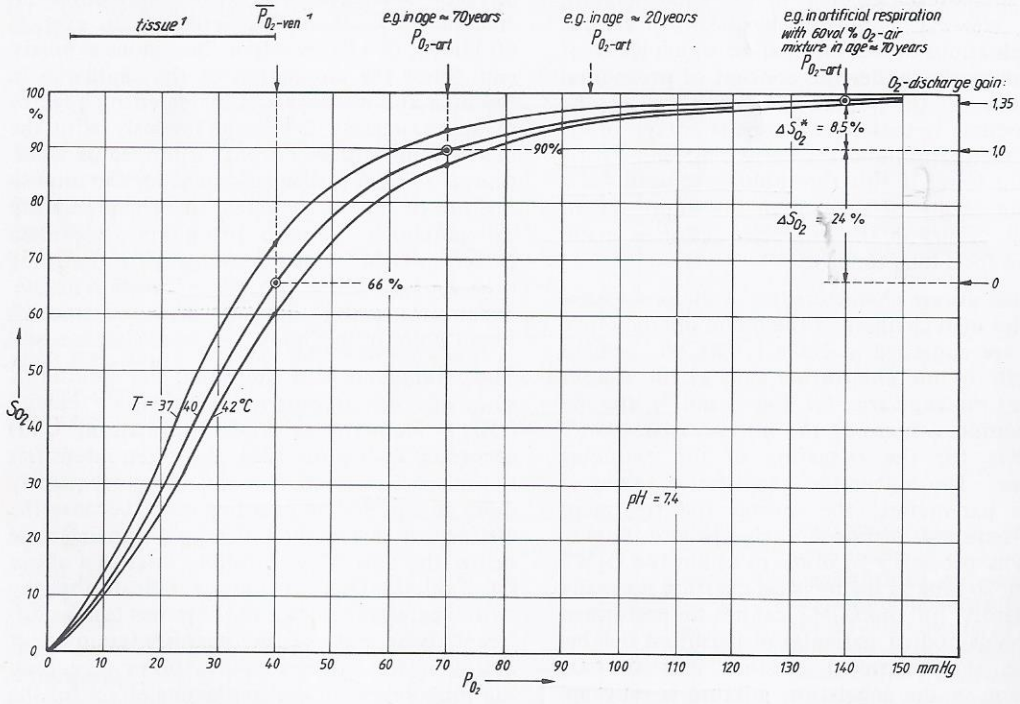


Fig. **124** Curves for O_2 binding in the blood as a function of oxygen partial pressure at 37, 40 and 42 °C. Example of the O_2 discharge gain S_{O_2} attainable in an elderly person with 40 °C fever (whole body hyperthermia), when O_2 content of inhalation air is elevated from 20 to 60 vol.-%, in the initial phase of the infection, $P_{O_{2\text{-ven}}}$ still remains almost constant

[1] For values in various organs see Fig. **9**

Similar results were obtained for numerous other cases with high fever in various clinics acting under the author's advice.

This O_2MT quick procedure, which can hardly be surpassed in its simplicity, deserves great attention because of its multivalent effect:

1. Circulatory support of the patient with high fever (risk reduction);
2. Reduction of time of recovery;
3. Reduction of working hours lost (in the interest of the patient, the employer and the medical insurance);
4. Charging of the host's defense system.

2.1.4 No poisoning by O_2 in O_2MT when the O_2 flow and the procedure duration are correct

Although oxygen is a blessing in intensive care units, in modern anesthesia, in emergencies and in O_2MT, it must always be remembered that O_2 poisoning can occur with a too high concentration of oxygen, or with respiratory gas mixtures with more than approximately 65 vol% O_2. The safety from O_2 poisoning is a question of the dosage as regards concentration and time.

It is stated in [32] that "in order to exclude the possibility of O_2 poisoning, respiratory mixtures with an O_2 concentration < 60 vol% and an O_2 partial pressure < 450 mmHg (60 kPa) are applied in longer lasting isobaric O_2 therapy in adults. In the treatment of newborn babies and infants, respiratory gases are used, the O_2 content of which must not be greater than 40 vol%, and the O_2 partial pressure not greater than 300 mmHg (40 kPa). Treatment with pure oxygen must be limited to approximately 4 h under normal pressure conditions."

In all procedural variants of the O_2MT the prescribed dosage of oxygen lies far below the toxic limit. The longest uninterrupted O_2 application is 7 h for the "5-night cure". O_2 is applied here during sleep via a soft mask applicator with storage balloon, with an O_2 flow rate adapted so that the O_2 concentration in the alveolar space of the lung is only approximately doubled. In the 2–4 h applications of O_2 during the individual sessions of the 36 h O_2MT procedure, the O_2 flow is always so adjusted that the O_2 concentration in the respiratory gas always remains below 60 vol%. Thus the regulation reported from [32] is observed with an additional safety factor in these procedural variants.

Pure oxygen or respiratory gas containing roughly 90 vol% O_2 is used in the 15 min O_2MT quick procedure. The 15 min application here remains very far below the aboved named 4-h limit, however, even with several repetitions of the treatment. In the O_2MT obstetrics procedure GK 2-IV, the dose of pure O_2 is limited to 120 min.

Dizziness and cramp are typical signs of O_2 poisoning. Changes in the alveolar membranes can be found in the lung, which can become a cause of diffusion disorders, increase in the proportion of shunt blood and accumulations of fluid in the alveoli (lung edema) [235]. In addition to this the COP is reduced as a result of increased vagotonia, and the circulation in the brain and kidneys is reduced. Numerous enzymes of the intracellular respiration are influenced. Thus, for example, the oxidation of glucose, fructose and pyruvate is inhibited in hyperoxia. The dangers of longer-lasting inhalation of pure O_2 in terms of progredient lung damage (total lung fibrosis as final stage) are shown in [236]. When a (toxic) dose of virtually pure oxygen is given for too long, the host's cellular defense is no longer stimulated, but reduced [237].

No detrimental effects have as yet been observed with very frequent 15 min O_2 applications, nor in the successful respective O_2MT variant over large periods of time (e.g. 10 years). Reference [238, 238a] should be mentioned in this context: it was found here in the framework of lifespan determinations using the Hayflick method, that the maximal cell division number was reduced to approximately 5% in cultures of human diploid cells (strain WI/38/ when the O_2 partial pressure in the cells was excessively raised from its normal level of around 15 mmHg (2 kPa) to 150 mmHg (20 kPa).

A positive consequence of the lasting improvement in the O_2 status for the non-specific cellular defense is the promotion of the formation of peroxides in phagocytosing cells (cf. Table **43**). In other areas of the organism (e.g. the lens of the eye), the increased formation of toxic peroxides or oxygen radicals could in theory have negative consequences. Such a view has occasionally been asserted against the O_2MT, but it was overlooked that the body has developed an efficient antioxidative protective system for such areas. Enzymes such as superoxide dismutase, catalase, and also glutathione and ascorbic acid are involved there. Investiga-

tions into this question were carried out in our Institute together with the Institute of Pathological Biochemistry of the Medical Academy of Dresden, by Klemm and Schaper [239]. The result was that immediately after O_2MT treatment (variant GK 4-I) an *increase of 50% in the antioxidative protective system superoxide dismutase (SOD) is measured in the red cells*, with only moderate decline in concentration in the course of 30–60 days.

2.2 Increase in the O_2 utilization capacity in the tissue by means of drugs (1st step)

2.2.1 Drugs and their dosage

The increase in the *O_2 utilization capacity in the tissue* can be defined as the improvement in the O_2 exploitation in the tissues and cells by means of the discussed capillary wall mechanism and drugs. The effect of this improvement is a reduction in the venous oxygen partial pressure $P_{O_{2\text{-ven}}}$, i.e. an increase in the arteriovenous saturation difference $\Delta S_{O_2} \triangleq \eta$, with unchanged

Table 12 Substances to increase O_2 utilization capacity in the tissues

No.	Substance	Area of influence in the organism	Biochemical place of influence	Dosage mg/kg	Dosage mg/70 kg	References (Remarks)
1	Thiamine (Vitamin B_1)	Whole body	Controlling of substrate flow into the Krebs cycle	0.43	30	2, 4, 242 (main drug)
2	Dipyridamol	Whole body	O_2 and glucose permeation (brain); 5% increase of blood flow (myocar.)	0.7	50	2, 4, 243
3	Magnesium orotate	Whole body	"Nucleic acid precursor", electrolyte carrier, brain cell	1.4	100	2, 4, 244
4	Thiamine (B_1) No.1 Dipyridamol 2 Magnesium orotate 3	Whole body	Combination preparation especially developed for O_2MT	Tablet Ø = 11 mm, 3 mm thick	30 50 100 180	Drug combination "Oxygenabund" (A. Herbert KG, Wiesbaden-Bierstadt)
5	Orotic acid (Vitamin B_{13})	Whole body	as for 3	1.4	100	2, 4
6	Pangamic acid (Vitamin B_{15})	Whole body		0.43	30	2, 4
7						
8						
9	Vitamin C	Whole body	Improvement in host's defense capacity	14	1000	2, 4, 245 (Advisable supplement to combination preparation no. 4)
10	g-strophanthin (perlingual from a 6% solution in the oleophile phase)	10.1 myocardium 10.2 blood-brain-barrier (BBB) and brain	co-use of lactic acid as energy substrate	0.09 0.17	6 e.g. 12 (simultaneously!)	146, 171, 179, 180 (pH raising effect) 182, 186, 187, 192

physical exertion. A compilation of drugs to improve the O_2 utilization capacity in the tissue can be found in Table **12**.

Vitamin B_1 (thiamine) is used in all variants of the O_2MT as the *main drug to improve the O_2 utilization capacity*. As a component of the cocarboxylase, it promotes the oxidative decarboxylation of pyruvate, which stems from the Embden-Meyerhof pathway, to acetic acid. This is then subject to complete oxidation to carbon dioxide and water in the citric acid cycle [240]. Thus vitamin B_1 increases the oxygen requirement from the substrate side and thereby its utilization capacity [241]. Thiamine is a naturally occurring substance in plants, animals and humans. In the form of thiamine pyrophosphate (TPP) it plays an important role in the terminal oxidative pathway of carbohydrates, as the coenzyme codecarboxylase. It thereby gains great significance for the energy turnover not only of the structures of the nervous system, but also for the musculature, especially the myocardium. It has long been known that the vitamin B_1 requirements are directly correlated with the intake of carbohydrates in food, and that not only a deficient supply of the vitamin in food, but most of all, chronic alcoholism, diabetes mellitus and gastric subacidity, lead to a relative vitamin B_1 deficiency. It was found in animal experiments (rats) that the first sign of TPP deficiency is a drop in the codecarboxylase concentration in the brain, which finally leads to a drop in the energy turnover. Vitamin B_1 substitution therapy has therefore been practised for decades, and still has a firm place in clinics today; the ageing person deserves particular attention here, as he is predestined to latent vitamin B_1 deficiency because of a frequently one-sided carbohydrate diet and an almost always existent gastric subacidity.

The O_2MT, which is originally intended for the elderly individual, therefore falls back on thiamine and proceeds from the consideration of abolishing the limiting influence of TPP in the energetic metabolism in the brain and myocardium, by means of mild surplus medication (single dose 30 mg). The direct proof, using animal experiments, of the correctness of this assumption came from our group (cf. Fig. **133**): combined with an increased O_2 offer, thiamine (hydrochloride) in the given dosage range is able significantly to raise the steady state concentration of the energy-rich phosphates ATP and CP in the rat brain. Thiamine thus evidently leads to an improvement in the O_2 and glucose utilization in the tissue.

A further substance used is *dipyridamol* (INN), which works via two different mechanisms. It increases the uptake and utilization of O_2 and glucose specifically in the brain [246]. Furthermore, in an increased dosage (2.2 mg/kg) the drug causes a roughly 5 % increase in the circulation (in the myocardium) for the duration of approximately 90 min [243, 247]. Dipyridamol was included in the therapy regimen of the O_2MT in order to use the described pharmacodynamic effects, namely in the brain and the myocardium, which lead to an improved circulation and an increased O_2 (and glucose) utilization. Like thiamine, dipyridamol's action could also be confirmed by animal experiments (cf. Fig. **133** and literature): In rats given 0.25 mg/kg (s.c.), an increase in the steady-state concentration of energy-rich phosphates in the brain tissue was achieved when the O_2 offer was simultaneously increased. Dipyridamol sometimes causes headache. This drug cannot be used in patients who react in this way (only 30 mg vitamin B_1 and 100 mg magnesium orotate should be administered, but not the combination preparation "Oxygenabund").

Another substance used is magnesium orotate, which is known due to its favorable effects on the cerebral functions, namely due to a certain prevention of age-conditioned cerebral changes ("nucleic acid precursor") [244, 248, 249]. The Mg^{2+} ion is essential for both the plant and animal organism. It plays a central role in the intermediary metabolism of carbohydrates and lipids, in the activation of numerous enzymes, also especially in synthesis and transfer of the energy-rich phosphates. Its interrelation with vitamin B_1 (TPP) is also interesting here. Mg^{2+} was accorded particular attention due to its inhibitory effect on vascular sclerosis in conjunction with a reduction of the serum lipid level (activation of lipases and cholinesterase), and also due to the observation that a Mg^{2+} deficiency evidently promotes the ageing of the organism.

The combining of Mg^{2+} with two orotic acid residues (uracil-4-carbonic acid) to form Mg orotate is founded on the known idea that a better intracellular exploitation (electrolyte carrier) of the magnesium could thereby be attained.

Magnesium orotate has therefore gained a firm position in the basic therapy for degenerative cardiac and vascular diseases, particularly vascular sclerosis, and is used increasingly in the elimination of latent Mg^{2+} deficiency in the elderly. For this reason it was included in the therapeutic program of O_2MT, after experi-

ments with animals in our group showed an increase in the energy-rich phosphates, in particular in creatine phosphate in the rat brain, under O_2 inhalation and an s.c. dose of 1.56 mg/kg orotic acid.

Vitamin B_1, dipyridamol and magnesium orotate with their standard dosage for O_2MT are combined in the "Oxygenabund" (manufactured by A. Herbert, Wiesbaden-Bierstadt, FRG) in a *single, easy-to-swallow tablet* with a diameter of 11 mm and a thickness of 3 mm. It can be seen from Fig. **126** in accordance with [250], that this drug combination caused *a drop in the mean $P_{O_{2\text{-ven}}}$ of 4.4 ± 2.0 mmHg*, 30 min after administration. This corresponds to a 6% gain in the O_2 binding capacity of the blood. The level of this gain, illustrated by Fig. **127**, was the reason to suggest in [252] the *preceding administration of such a combination preparation in order to increase the effect of exercise training of all kinds*.

The example in Fig. **128** shows that the measured P_{O_2} increase in the tissue due to the pharmacological steps is to be regarded as a considerable contribution, alongside the effect of O_2 supply.

One drug which is given or can be useful as an adjuvant medication, usually in a high dosage and in conjunction with vitamin C, in various O_2MT variants (e.g. KA 1), is nicotinic acid. In its flush phase it increases the $P_{O_{2\text{-art}}}$ (Fig. **126**) for approximately 50 min, and can therefore be used in special cases to achieve a higher $P_{O_{2\text{-art}}}$ under O_2 application at the start of the treatment cycle. A cup of coffee has the same indication and, as Fig. **30** above shows, a similar effect (with greater variation).

As a substance to increase further the O_2 utilization capacity specifically in the myocardium and in the brain, g-strophanthin is used [150, 155], the extraordinary pharmacokinetics of which were discussed in 1.2.3. It was seen that

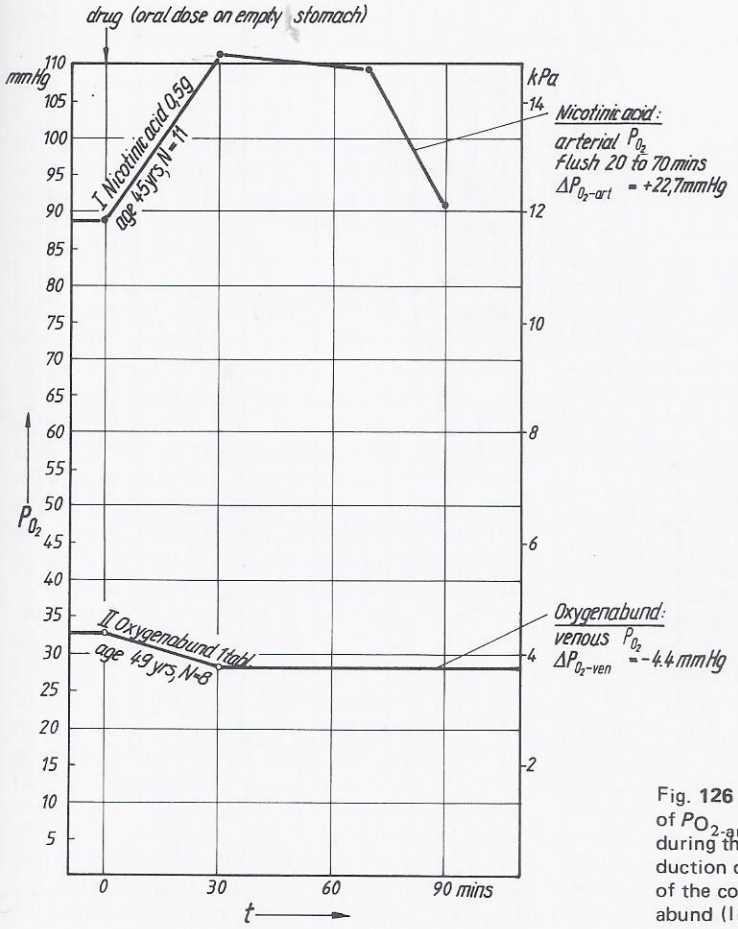


Fig. **126** Measurements showing the increase of $P_{O_{2\text{-art}}}$ by means of 0.5 g nicotinic acid during the flush phase (I) and a long-term reduction of the $P_{O_{2\text{-ven}}}$ by means of 1 tablet of the combination preparation Oxygenabund (II)

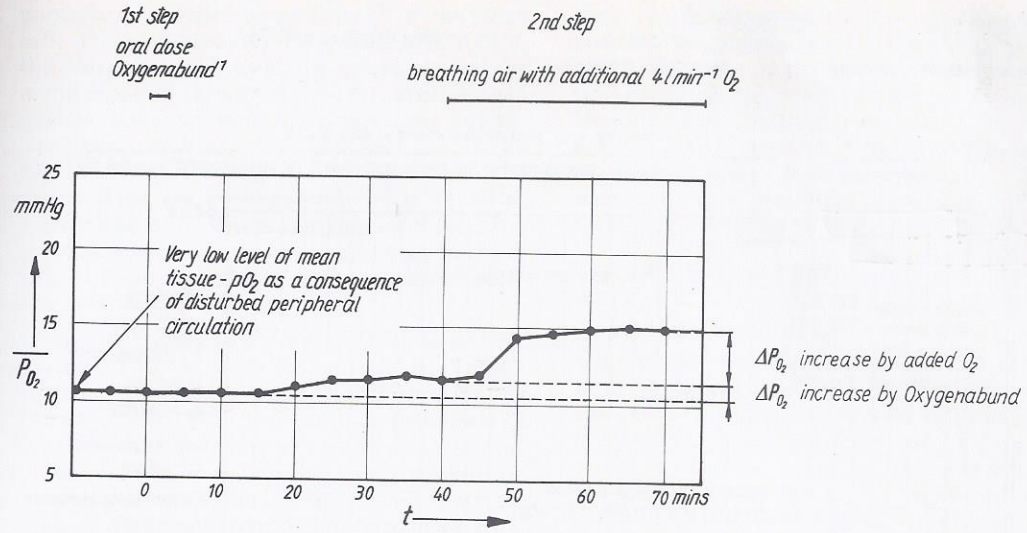


Fig. **128** Measurement, using a large-area P_{O_2} electrode, of the mean P_{O_2} level in the big toe of a 72-yr-old patient with circulatory disorders in the same leg, after oral dose (empty stomach, morning) of Oxygenabund (1st step) and after addition of 4 l·min^{-1} O_2 to the breathing air (2nd step)

[1] Composition: 30 mg vitamin B_1, 75 mg Dipyridamol, 100 mg magnesium orotate

perlingually administered g-strophanthin has a reliable and strong effect, if the glycoside in an amount of 6 (or 12) mg and in a high concentration (c = 6 % in the oleophilic phase), is put on the dried tongue.

It can be gathered from our present ideas on the temporal concentration course of g-strophanthin in the blood circulation, summarized in Fig. **129**, that:

1. Since, under the given concentration conditions, the time constants of the binding of g-strophanthin to the receptors in the tissue are, according to [252], only fractions of a second, the effective bloodflow time to the receptors determines the elimination of the drug from the blood circulation (blood circulation time $t_c \approx 1.5$ min). This explains the extraordinarily *small time constant of the evasion of g-strophanthin from the circulation*, $\tau_{evas} \approx 0.5$ min [148].

2. For the binding of g-strophanthin to the receptors of the myocardial cell membrane, the given *dose proportion* is decisive, according to [252] and contrary to earlier ideas [179]. This means the triggering of the metabolic switching effect of g-strophanthin, postulated in [179] and proven in [146] (longer lasting, pH-increasing effect), as soon as a certain number of glycoside molecules (dose proportion, integral value) are brought to the receptors, and not as soon as a certain glycoside concentration in the blood is exceeded.

3. In perlingual administration, between roughly the 2nd and 18th minutes after administration, *a small, but after 6–10 min still highly cardioeffective proportion* (e.g. 0.19 mg, almost the same amount as in i.v. injection) of the administered dose (e.g. 6 mg) goes *directly into the blood circulation*. This process can be termed "primary invasion phase" (I in Fig. **129**).

4. When given perlingually, by far the *greatest proportion of the dose* (70–85 %) is at first *bound rapidly in the tongue tissue* and stored there [252]. After a timespan determined by the dissociation time constant ($\tau_{diss} \geq 120$ min) [25], the bound high dose proportion (e.g. 5 mg) goes slowly into the blood circulation. This leads to the remarkable reincrease of g-strophanthin concentration in the blood circulation, specific to perlingual administration, beginning 2 h after application [253, 254]. It was shown in [148] that the evasion time constant increases from 0.5 min during the primary invasion phase, to 4 min during the second invasion phase. It follows from this that, in the dissociation process, a change occurs in the binding structure of the g-strophanthin molecule, which can explain the observed fact that the

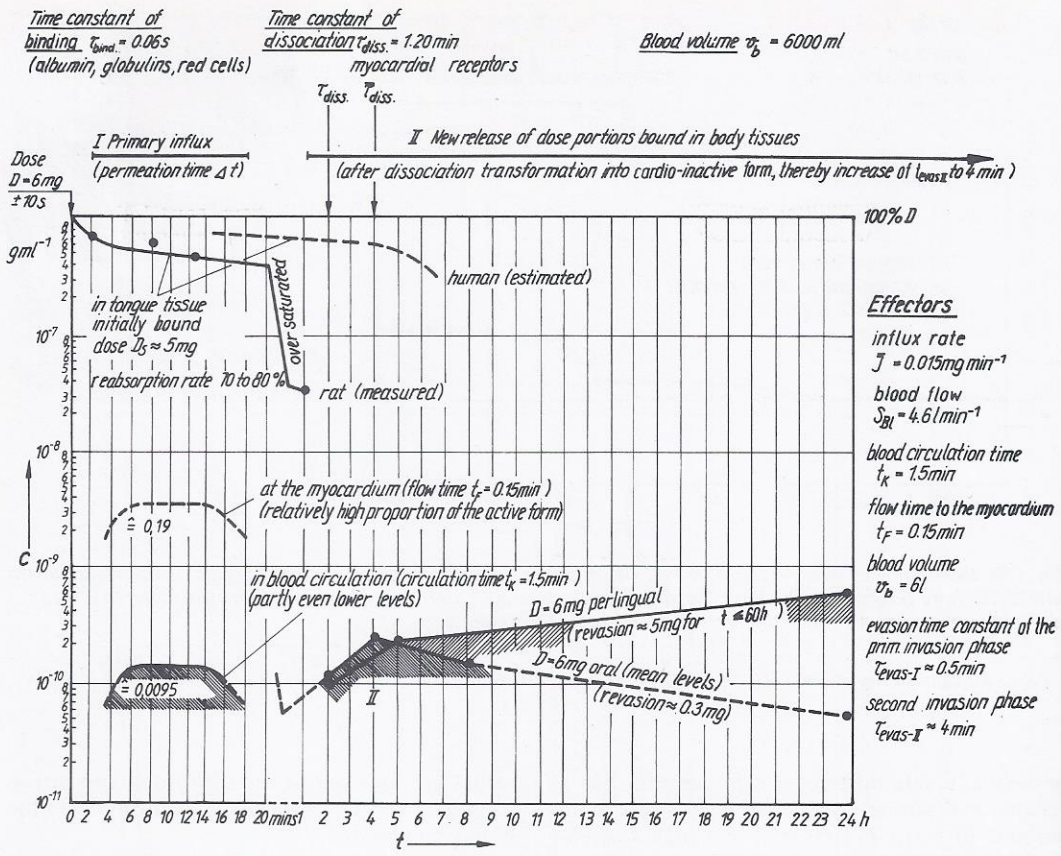


Fig. **129** Measurements and ideas derived from these [179, 180] of the time-dependent concentration profiles of g-strophanthin in the blood circulation after a perlingual 6 mg dose from a biteable capsule with a high strophanthin concentration [252] (Strodival special capsule). I. Primary influx phase (fast action with only slight variation of effect); II. Secondary influx phase (release, re-activation, inactivation) [148]

drug becomes cardioinactive and has low toxicity in the secondary invasion phase.

Perlingually administered g-strophanthin deserves great interest for O_2 deficiency in the myocardium because, when administered early enough by the patient himself, it can quickly ameliorate the dangerous reduction in the blood microcirculation or even eliminate it [122] due to its pH-increasing effect [148] in the deficiency area. *The certain and rapid cardiac effect of g-strophanthin applied perlingually from a 6 mg – 6% preparation* (Strodival special) *has recently also been proven in a clinical study with large numbers of patients of an out-patient department* (complete arrest of angina pectoris attacks within 5 to maximum 10 min after medication; failure rate only 15%) [147]. In special cases determined by the doctor (exercise ECG) the Strodival special preparation is also given 10 min before the start of the 15 min O_2MT quick procedure, GK 2-I.

2.2.2 Experimental results of increase in the O_2 metabolism during treatment. Rise in concentration of energy-rich phosphates in the brain

The concentration of the energy-rich phosphates in the brain as an indicator of the increase in the O_2 metabolism in the tissue by means of steps of the O_2MT. With Lohmann's discovery of adenosine triphosphate (ATP) and the discovery of the creatine phosphate (CP), the basis was formed for the recognition of the comprehensive significance of the energy-rich

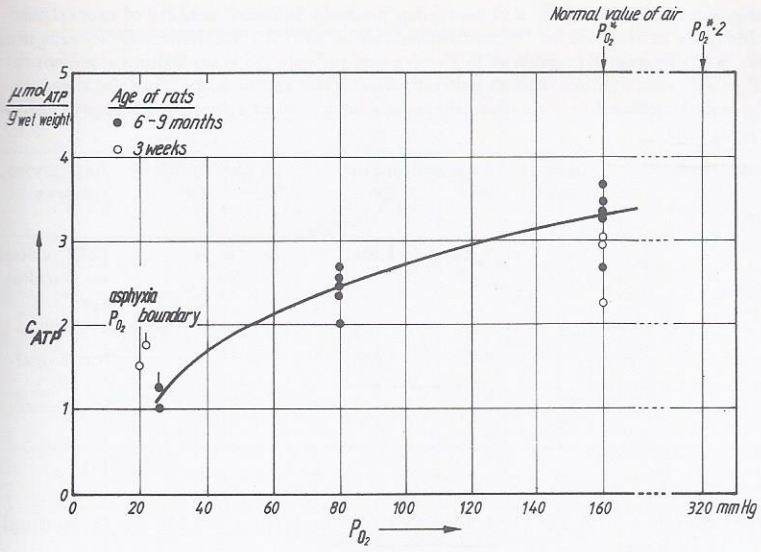


Fig. **132** Measurement of the stationary ATP concentration in the brains of rats as a function of the oxygen partial pressure P_{O_2} of the inspired air. (exposition time 60 min) [4]. 1 mmHg = $1.33 \cdot 10^2$ Pa

calculated as a percentage of the standard concentrations of the control animal = 100 %.

Results on the dependence of the ATP content of the brain cells on the long-term P_{O_2} of the inhalation air. Measurements of the steady state ATP concentration in the brain as a function of the oxygen partial pressure are summarized for rats (N = 17) of the two age groups named, in Fig. **132**. The influence of age could be seen particularly clearly in the case of the asphyctic P_{O_2} border. Here the 3-week-old rats had, with a lower P_{O_2} (20 or 22, as compared with 26 mmHg), an ATP concentration in the brain which was higher by a factor of about 1.5. This result confirms earlier findings, according to which older animals are more sensitive than younger ones to oxygen deficiency.

During the incubation period the animals remained under changed P_{O_2} long enough for it to be certain that steady state conditions had formed as regards the ATP concentration in the brain (120 min). The course of the curve obtained under these conditions shows a considerable increase in the ATP concentration in the brain when the P_{O_2} level rose from 30 up to 320 mmHg. The doubling of the P_{O_2} of the inhalation air from about 150 to 300 mmHg is a goal of the O_2MT. In order to simulate with laboratory animals the older human organism with its cardiopulmonal performance reduced to 50 % for example, rats aged 6–9 months were used and kept over a longer period of time at a P_{O_2} level that was roughly half that of normal air (80 mmHg). Under these conditions, the $P_{O_{2\text{-art}}}$ of the animals was around 70 mmHg.

Measurement of the increase in concentration of the energy-rich phosphates in the brain after the P_{O_2} of the inhalation air has been doubled and after administration of various drugs to improve the O_2 utilization capacity. According to [4], stationary concentration relations are reached after 30 min when the P_{O_2} is raised from 80 to 160 mmHg, and after 90 min when it is raised from 160 to 320 mmHg. Table **13** shows the *extent of the increase in the concentration of energy-rich phosphates in the brain* (correlation with the increase in O_2 metabolism) *after the P_{O_2} of the inhalation air has doubled, and after administration of various drugs or drug combinations.* These measurements prove that the dose of drugs to improve the O_2 utilization capacity (1st step of the O_2MT) brings about a significant additional increase in the concentration of energy-rich phosphates in the brain, e.g. ATP from 140 to 160 % with the simple combination of vitamin B_1 plus dipyridamol. The results given in the table form the basis for the choice of the drug combination according to type and dosage (e.g. combination preparation Oxygenabund) in the 1st step of the O_2MT.

The slow fading of the concentration of ATP and CP, over a period of 4 h, which can be seen from the measurements compiled in Fig. **133**, is surprising. This is a *further fundamental effect of the O_2MT.* This result led to *the 90 min O_2MT variant being carried out immediately before severe stress.* In this way, for example, extraordinary circulatory stability was recorded during brain operations of several hours' duration.

Table **13** Gain factors of the energy-rich phosphates ATP and creatine phosphate (CP) in the brain of rats 30 min after increase of the P_{O_2} in the inhalation air from 80 to 160 mmHg combined with the application of various drugs to improve O_2 utilization capacity. The high gain attainable with the drug combination (4) underlines the importance of even the first step of the O_2 multistep therapy. A high gain can also be derived directly from the measurements in Fig. **126** (reduction of the mean venous P_{O_2} = -4.4 mmHg by the drug combination Oxygenabund containing Mg orotate, thiamine and Dipyridamol)

Drug	number of animals	application	time	Dose D mg/kg	total gain factor ATP	total gain factor CP	drug gain factor[1] ATP	drug gain factor[1] CP	References, remarks
1 30 min sleep with normal P_{O_2} in the inhalation air					1.12	1.29	–	–	[242] values for middle-aged animals
2 30 min doubling of P_{O_2} in the inhalation air	30				1.40	1.62	–	–	(no drugs)
3 like 2, but with drugs:									[4]
3.1 Thiamine (vitamin B_1)	6	i.m.	20 min before doubling of P_{O_2}	0.34	1.50	1.73	1.10	1.11	(main drug)
3.2 Dipyridamol (Persantin®, Curantil®)	6	i.m.	as 3.1	0.5	1.52	1.80	1.12	1.18	
3.3 Orotic acid (vitamin B_{13})	6	i.m.	as 3.1	1.56	1.47	1.84	1.07	1.22	(usually given as magnesium orotate)
3.4 Pangamic acid (vitamin B_{15})	6	i.m.	as 3.1	0.446	1.48	1.74	1.08	1.12	
4 *Thiamine + Dipyridamol*	6	i.m.	as 3.1	0.17 + 0.25	*1.60*	*1.82*	*1.20*	*1.20*	[4]

[1] Gain factor of P_{O_2} doubling subtracted

2.3 Increase in the blood supply of tissue (3rd step)

2.3.1 Significance of the blood flow for the attainment of a lasting improvement of η by means of the O_2MT

The oxygen multistep procedures can only be successfully performed when there is a good blood flow in the tissue (good circulatory condition) and, particularly, when the circulation is increased by means of physical exertion or in some other way. For this reason the *3rd step*, discussed in this paragraph, *is an obligatory component of the O_2MT*. As was already discussed in Paragraph 1.1.1, the desired high-charging of the microcirculation occurs when the P_{O_2} in the venous part of the capillary network is increased during O_2 application to approximately 50–60 mmHg (6.6–8 kPa) (cf. Fig. 3), and when, simultaneously, the circulating volume $\dot{Q}$ is high (cf. Fig. 57). Because of the influence of endothelial cell swelling on the narrowest capillary cross-section and therefore also on the circulating volume, these two parameters are functionally bound to each other. Nevertheless, it can be stated that *the higher nutritive capillary perfusion in the organs important for the elementary vital functions (lung, respiratory musculature, heart) the less oxygen and procedure time are needed to achieve the aimed-for high-charging of the microcirculation.*

2.3.2 Increase in the blood flow in lung and heart by means of physical exertion

Figure **134** gives information on the *increase in the cardiac output* occurring in normal persons in *increasing physical exertion* (measured in watt). It can be seen from this presentation that the *circulation* in the two elements involved in the respiratory function (lung, respiratory musculature), and in the myocardium, increases by a factor of around 2 during physical exertion of 100 watts. As a rule, the $P_{O_2\text{-art}}$ then also increases with a typical course, as the example in Fig. **135** shows. An example of the approximate connection between cardiac output and pulse frequency f can be found in Fig. **136**.

A very great increase in the RMV with exertion occurs simultaneously with the increase in cardiac output (see Fig. **137**). At an exertion of 100 watts, for example, the RMV has risen by a factor of 4.7 compared with the level measured at rest. In order to ensure that the O_2MT procedure employed has full effect, the *flow of the respiratory gas mixture containing 40, 60 or 90 vol% O_2 is to be adapted to the RMV of the chosen physical exertion*. When, at an exertion

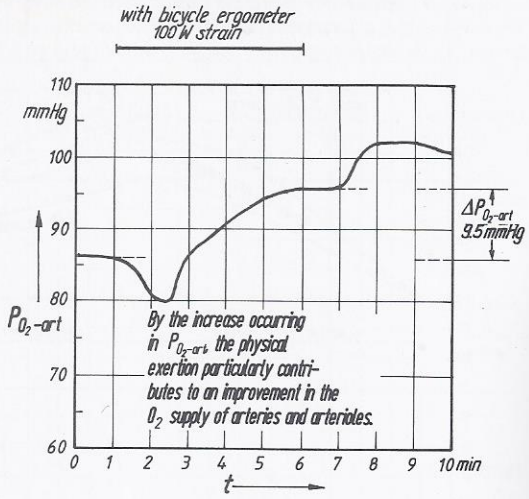


Fig. **135** Mean values of four transcutaneous registrations of the arterial P_{O_2} at a physical strains of 100 W in four healthy individuals. 1 mmHg = $1.33 \cdot 10^2$ Pa

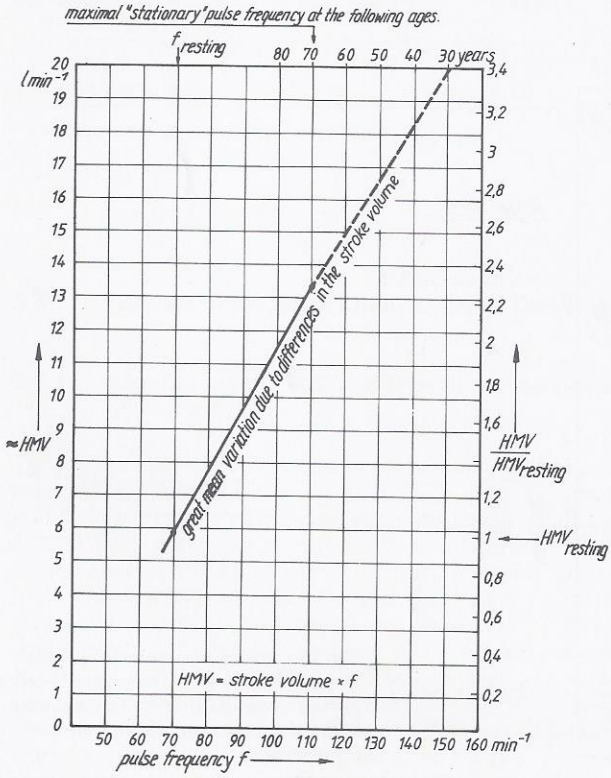


Fig. **136** Relationship between pulse frequency f and heart minute volume HMV. Approximate mean values at normal conditions according to [106]. The age-dependent decrease of the minute volume is reflected by the upper scale of the maximal "stationary" pulse frequency. In O_2MT these values can be temporarily exceeded

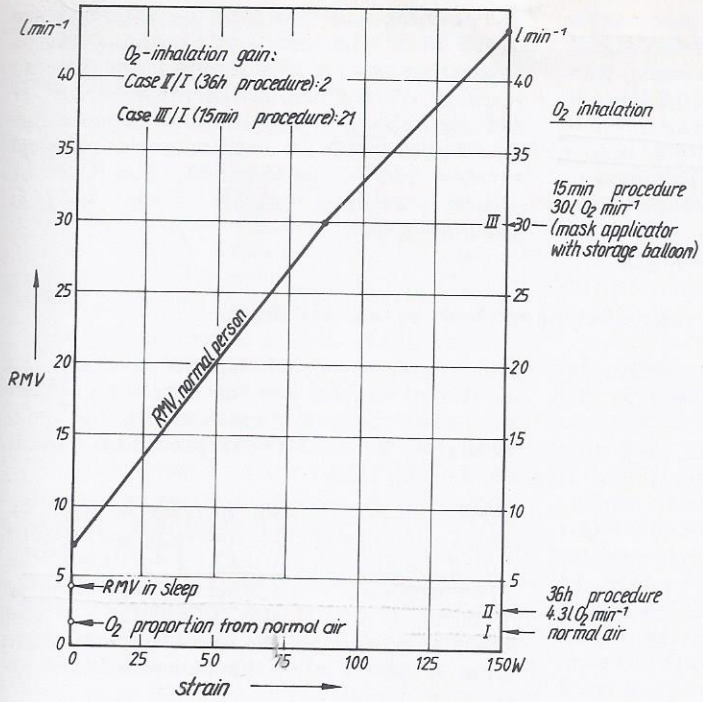


Fig. **137** Respiratory minute volume RMV of normal individuals dependent on physical strain; guidelines

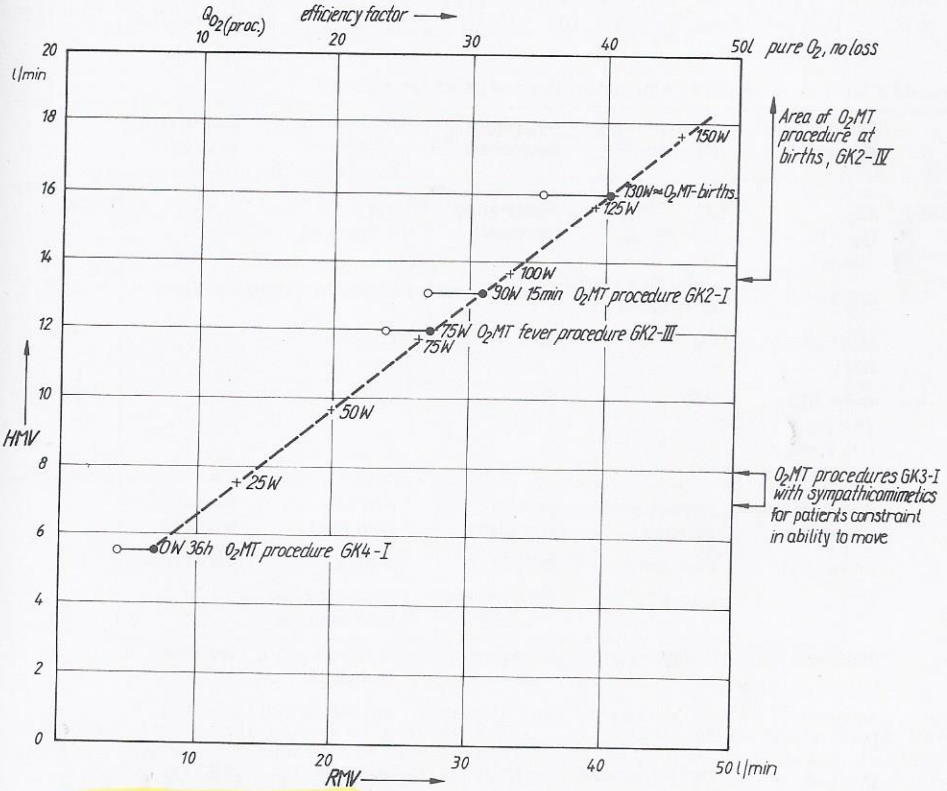


Fig. **138** Heart minute volume HMV, respiration minute volume RMV and O_2 flow rates needed for the different O_2MT procedures ($Q_{O_2\,(proc)}$) in dependence on physical strain given in watts during various O_2MT treatment variants

of 100 watts and application of pure oxygen (quick procedure), this adaption is established, the O_2 supply to the lungs, for example, is increased by the product $4.3 \cdot 4.7 = 20.2$ (!) compared with normal conditions. In this example the amount of O_2, increased 20-fold, is to a large extent taken up by the lung. This explains why the named exertion can also take place in conditions of weakness.

The occurrence of an over-proportional increase in the RMV with increasing exertion (without application of O_2) is a sensitive sign for the reaching of the aerobic-anaerobic border of exercise training. The relationship between cardiac output and RMV as a function of physical exertion and the pertinent O_2 flow rates of various procedural variants of the O_2MT is given in Fig. 138.

2.3.3 Increase in the circulating volume in lung and heart by means of drugs

In physically disabled or non-able-bodied patients, who are particularly in need of the O_2MT due to the long-term distress of "exercise deficiency", the increasing of the circulating volume $\dot{Q}$ by means of drugs presents itself as a solution. Substances which increase cardiac output (COP) for 2–6 h have been known for a long time, certain doping substances banned for competitive sportsmen, for example. Table 14 shows a compilation of the COP-increasing effect of various sympathicomimetics [256–259]. The increase in COP attained in this comfortable and well tolerated way does not reach the level attainable by physical exertion in fully able-bodied persons. It is sufficient, however, in order to design O_2MT variants in which the number of sessions and the total time needed are greatly reduced compared with the parameters of the 36 h O_2MT procedure, variant GK 3-I (Fig. 138).

O_2MT procedures with increase in COP by means of drugs should always be carried out during the morning, as the long duration of the effect afterwards could otherwise cause sleeping problems. It should also be pointed out and noted that, due to the side-effects of these drugs (euphoria etc.) the patient's fitness to drive is reduced.

It is known that a stimulation of the sym-

Table 14 Different effects of various sympathicomimetics and psychostimulants

Parameters	Orziprenalin[1] Alupent®	Amezinium Regulton®	Mesocarb Sydnocarb®	Amphetaminil AN1®, Aponeuron®	Dopamin analogues USA	
increase in cardiac output	35 $D_1 = D_2 =$ 20 mg	22 D = 30 mg	moderately increased	not influenced	~ 40	%
pulse rate	increased + 14 %	not influenced or reduced	hardly increased	hardly increased	increased	min^{-1}
onset of effect	after 30 min (D_1)	20	20	20		min
duration of effect	from 30 to 75 min (D_1) (D_2 necessary for a 2 h sitting)	300	300	420		min
drug type	β sympathicomimetic	sympathicomimetic	psychostimulant	psychostimulant	sympathicomimetic	
effect	peripheral	peripheral	central	central	peripheral	
receptors	β	α and β_1	CNS neurons	dopaminergic CNS neurons		
blood pressure systolic	increased amplitude + 30%	increased	increased	hardly increased	increased	
blood pressure diastolic	lowered	increased	not influenced	not influenced	lowered	
breathing	slightly increased	not influenced	centrally increased	centrally increased	slightly increased	

[1] Noticeable reduction of most side-effects when used in combination with the O_2 multistep procedure

pathicoadrenergic system with the aim of increasing the COP is accompanied by an increase in the O_2 consumption of the heart muscle. Functionally limited compensations in the framework of a chronically ischemic heart disease are therefore a contraindication, not only for the O_2MT variants with physical exertion, but also with drug stimulation of the COP. This also applies to arterial hypertonia (danger of provoking a hypertonic crisis), visual field contractions (glaucoma simplex), psychotic disturbances and prostate adenomatosis.

Sympathicomimetics should only be prescribed to patients in the framework of O_2MT under observation of the relevant contraindications and instructions given in the respective pharmacopoeia, i.e. not in agitated psychoses, thyreotoxicosis, prostate adenoma, contracted visual field or in severe myocardial diseases such as cardiac insufficiency, severe angina pectoris etc., or in severe hypertonia. The interaction of beta blockers and the drugs mentioned must also be observed here.

In some patients with reduced functional cardiovascular reserves, the administration of such drugs will only be possible *in the progression of an O_2MT treatment cycle* or *even not until a second O_2MT procedure*, when a preceding successful treatment has caused these reserves to have been built up again.

We selected orziprenalin (Alupent), examined in Fig. **139**. The measurement of the increase in O_2 uptake after perlingual administration of one 20 mg Alupent tablet (D_1) shows that a sharp drop in the heart effect sets in 75 min after application. For this reason, in a session lasting 2 h, a further 20 mg tablet (D_2) is usually given at t = 45 min, to secure a sufficient Alupent effect until the end of the session. The interesting observation can be seen from Fig. **139** (curve I) that, as a result of the O_2 application, the otherwise occurring critical drop in Q_{O_2} to below the expected level (curve II) does not occur. Thus the main side-effect of Alupent is eliminated. The organism's energy reserves are not critically drawn upon, because more chemical energy is formed in the first effective phase.

If the known relation between physical exertion and COP is used as a basis, the sympathicomimetic of the stated type and dosage is then equivalent to an additional physical exertion for the heart of 30 watts as can be seen from Fig. **140**.

Without the combination with steps 1 and 2 of the O_2MT, i.e. used alone, the sympathico-

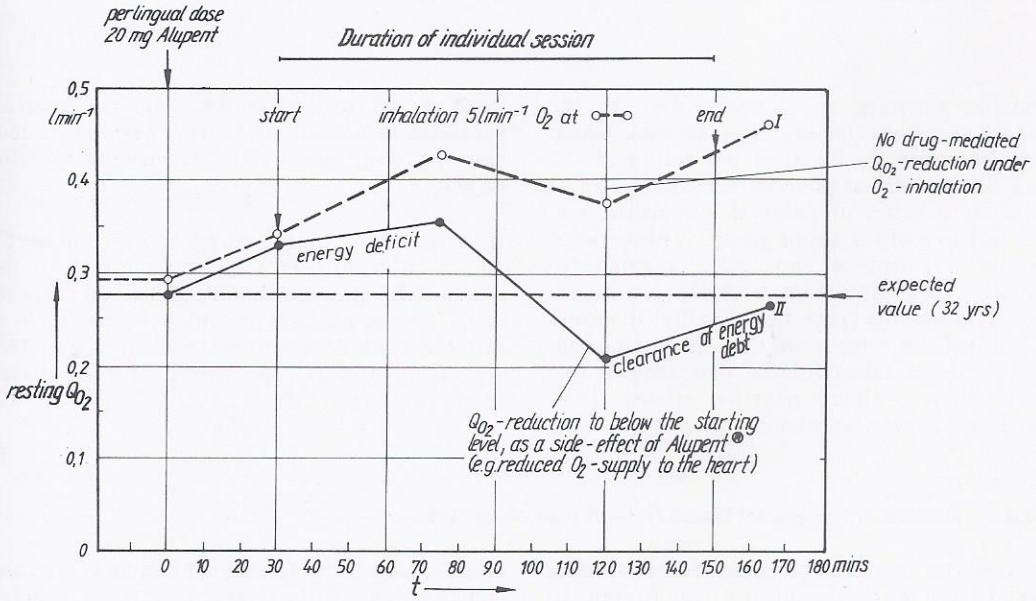


Fig. **139** Examples of the change in the O_2 uptake $Q_{O_2 at rest}$ after a single perilingual dose of 20 mg Alupent with (I) and without (II) inhalation of 5 l min^{-1} O_2. In case I the O_2 inhalation was each time interrupted for 8 min for the determination of Q_{O_2}. Result: the drop in Q_{O_2} to below the starting level (normal level) between t = 100 and 120 min (main side-effect of Alupent) disappeared when additional O_2 was given according to the O_2MT program GK 4-II

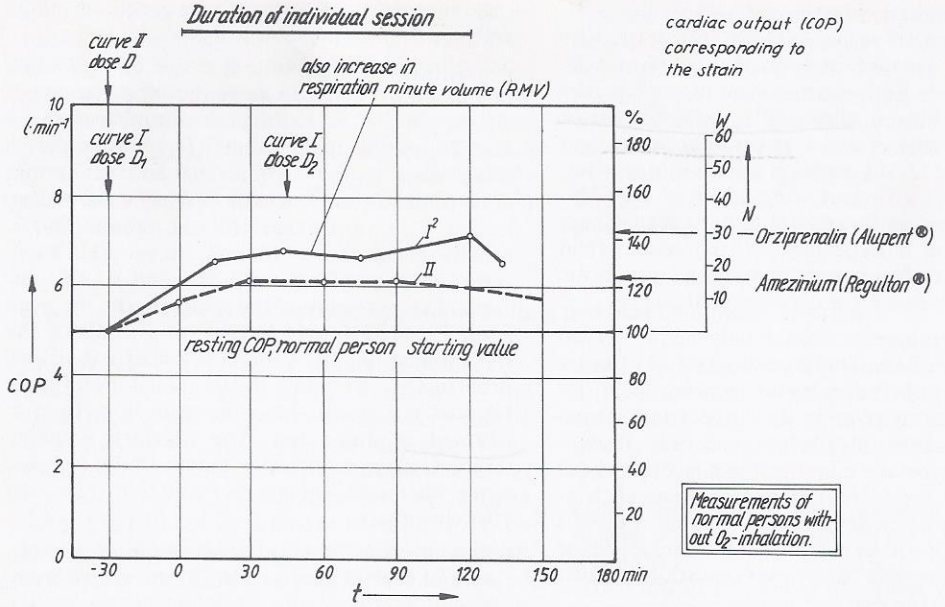


Fig. **140** Temporary increase in the cardiac output (COP) by means of sympathicomimetics, and their cardially effective portion expressed as a certain physical strain N. I = Orziprenalin (Alupent®), D_1 = 20 mg perlingual[1] at t = -30 min. D_2 = 20 mg at t = 45 min; II = Amezinium Metilsulfat (Regulton®) D = 30 mg oral

[1] Great weakening of most of the side-effects during the O_2MT procedure
[2] This curve is even higher when 5 l min^{-1} O_2 is inhaled (except during determination of Q_{O_2})

mimetics generate an energetic debt in the human organism (feeling of weakness), which must be made up for after the action of the drug. Similar cardiac (side-)effects are known to occur in a series of cerebral stimulants, e.g. such as those of the amine group. A new era for the use of peripheral and central sympathicomimetics in combination with O_2 can be expected to emerge from this. Finally, it should be pointed out once more that the doping substance can be taken for the first time in this combination without negative effects. Inasmuch as doping substances mentioned here leave a psychic dependence in the patient (problem of addiction), there is never any question of their use in the framework of the O_2MT.

If this option exists, physical exertion is of course preferable as a natural method to increase COP. It is worthwhile in special cases to adapt to the physical potential by means of a suitable type of exertion (manual ergometer, e.g. from Ballert, Ennigerloh, FRG; special rowing devices etc.).

2.3.4 Normal and maximal blood flow of various organs

In efforts to increase the circulation in specific areas of the whole organism it is important to know to what extent the tissue blood flow in the individual organ can be increased by means of vasodilatory control. Figure **141** gives information on this. As is to be expected, the maximal increase in bloodflow occurs in vascular areas in which the functional demands are subject to a particularly great change (skin, skeletal muscle, gastrointestinal tract, lungs, myocardium, liver, central nervous system). It is striking that the blood flow in the skin area can rise by a factor of up to 36. It is known that the size of this margin forms the basis of

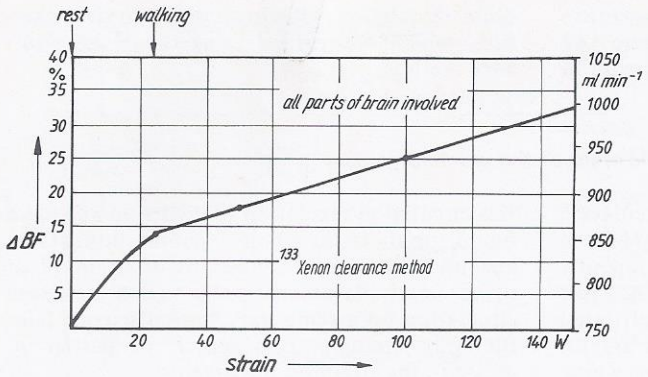


Fig. **142** Increase in brain circulation (blood flow BF) during physical strain according to W. Hollmann (personal communication of 3.8.1985)

organism adapts itself to the new situation mainly by an increased blood flow, that is, by an increase of the regional substrate supply. Because of the dependence of the flow resistance on the 4th power of the vessel radius (Hagen-Poiseuille's law), the regulation of the blood flow rate in the tissue by means of the related mediators occurs mainly by changes in the cross-sections of the vessels and, to a far lesser extent, by arterial pressure changes. The decisive vessel diameter is thereby mainly determined by the momentary state of contraction of the smooth vessel musculature in the precapillary area (terminal arteriole segments, resistance vessels). This contractile state gives the vessel wall an active tension, the so-called vasotonia. An increase in the state of contraction causes a decrease in the vessel diameter (vasoconstriction) and vice versa, i.e. a decrease in the state of contraction causes an increase in the vessel diameter (vasodilation). By means of the control of the relative flow resistance in the so-called *precapillary sphincters*, the distribution of the cardiac output to the individual organ circulation, connected in parallel, and the strength of the blood flow within individual

Table **15** Blood flow in various organs and cardiac output at physical rest and during different physical strains. Adapted from [32] and Fig. **141**

Vessel area	Blood flow (ml/min)				
	Rest	Light work (≈ 50 W)	Heavy work (≈ 150 W)	Maximal work	Remarks
Viscera	1400	1100	600	300	
Kidneys	1100	900	600	250	
Brain	750	880	1000	1400	855 at 25 W (walking)
Coronary	250	350	750	1100	therapy target
Arterial blood vessels (with vasa vasorum)	basic value	increased			therapy target
(Lung)	basic value	≈ 1.4 X basic value	3 X basic value	4 X basic value	therapy target
Skeletal muscle	1200	4500	12 500	22 000	(including lung musculature)
Skin	500	1500	1 900	600	
Other organs	600	400	400	100	
Cardiac output	5800	9500	17 500	25 000	ml/min
Arterial P_{O_2}	basic value	increased	strongly increased		

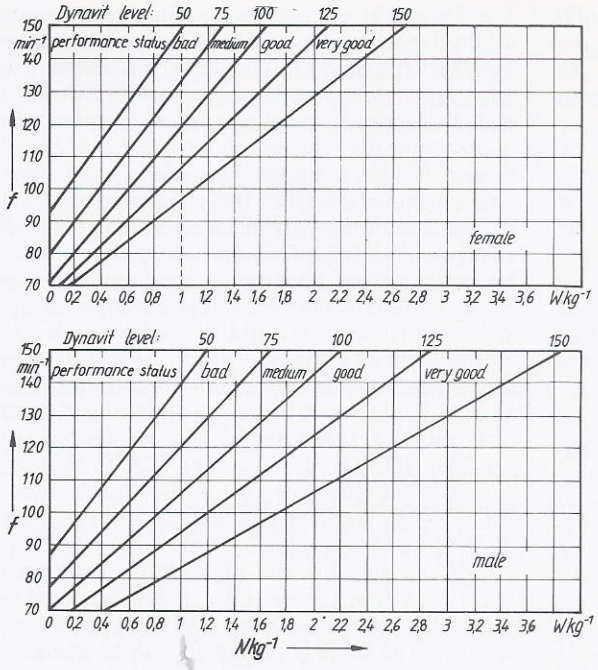


Fig. **145** Connection between specific exercise performance (watt per kg body mass) and the pulse frequency f at various performance levels of the human organism

Note posture

Fig. **146** Bicycle ergometer for defined strain and measuring of pulse frequency, performance status etc. during procedure of O_2MT. (Keiper Training Systems, Rockenhausen/ Pfalz, FRG)

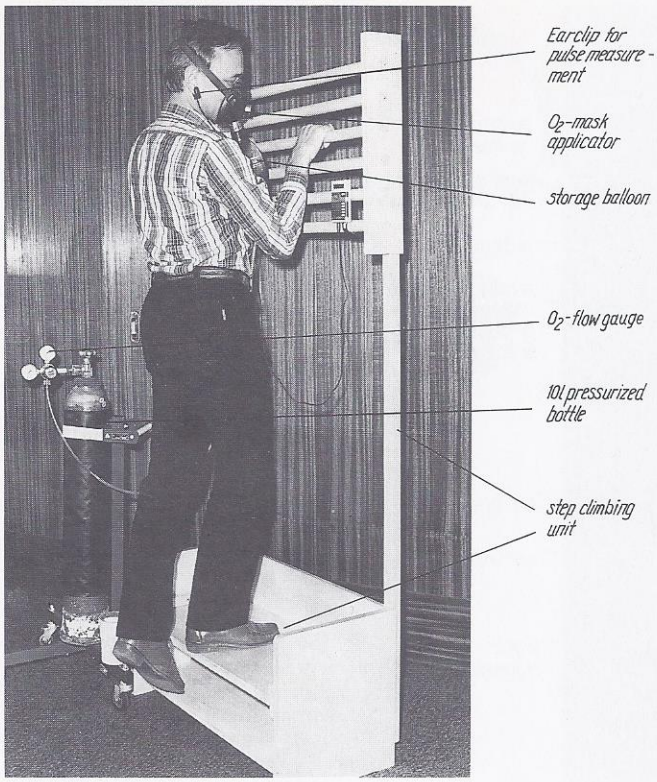


Fig. **151** Implementation of the 15 min O_2MT quick procedure with Kaltenbach's step-climbing unit. Adjustment of climbing frequency according to the prescribed training pulse frequency

and disabled patients. The simple manual ergometer with watt display, and hand instruments with selectable degree of exertion such as in Fig. **152** have been developed for this.

In connection with this attention should be drawn to a movable unit[1] for O_2MT, with which the physical exertion occurs with the aid of a swivelling ergometric part according to the crank ergometer principle (cf. Appendix).

2.3.6.3 Methods and aids for the implementation of physical exertion in exercise training and in transition to a more energetic lifestyle

It was shown in [37] that the deterioration of the O_2 status with advancing age can be traced back to the reduction in cardiac output. For this reason the combat of this reduction by means of exercise training is one of the most important measures for the maintenance of health in old age. The task consists of maximally increasing the cardiac output and afterwards keeping it high on a long term basis, but with the minimum amount of time and effort. In order to fulfil this damand, the O_2MT program plans *exercise training* on the one hand, and a transition to a *more energetic lifestyle* on the other.

The training must take place in both phases without application of O_2, as the desired training effect only occurs when the energy metabolism reaches the aerobic/anaerobic border (stimulus required for the sprouting of blood capillaries) [269, 270]. Because the training takes place without O_2 application it can be carried out either with stationary systems, or in a nonstationary way. For the same reason the training is not timebound to the interval of the main procedure of the O_2MT. Despite this, a *minimal training* [270] *of 10 or 2 x 5 min* without O_2 application was placed at the end of the

[1] Manufactured by Battert, Ennigerloh, FRG. The device consists of a 2 x 10 l pressure cylinder unit, O_2 flowmeter up to 40 l/min, electronic pulsemeter, exertion display etc. The crank ergometer is also suitable in most cases for disabled and paraplegic patients

Fig. **152** Technical aids for the implementation of short O_2MT variants for partially movement-disabled patients (e.g. bedridden). Use of the low-loss O_2 mask applicator with storage balloon and, in the foreground, a hand apparatus (impander) with adjustable strain. On the right a 10 l pressure cylinder with reducing valve and special O_2 flow gauge up to 30 l/min

Table **17** Several physical activities and their mechanical equivalents N on a bicycle ergometer (normal person, BW = 70 kg, height 1.80 m, male; approximate figures)

No.	Type of movement		N in watt
1	walking slowly	2 km/h	4
2	playing with children		15
3	walking	4 km/h	22
4	cycling without head wind	10 km/h	23
5	walking quickly	5 km/h	29
6	playing skittles (mean in time)		31
7	gymnastics		62
8	tennis (mean in time)		62
9	swimming (backstroke)	23 m/min	62
10	golf		64
11	dancing (foxtrot)		66
12	table tennis		70
13	pulse from 70 to 100/min (for < 80 years)		75
14	canoeing	126 m/min	93
15	pulse from 70 to 110/min (for < 70 years)		100
16	cross-country skiing	4 km/h	113
17	step climbing (height of steps 17 cm)	60 st/min	116
18	horse riding (gallop)		136
19	marathon running	9 km/h	142
20	swimming (breast stroke)	50 m/min	162

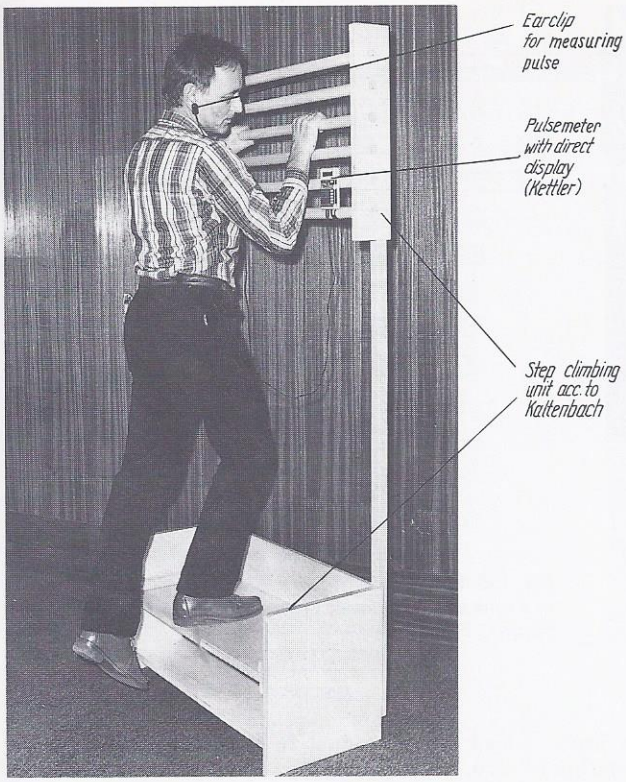


Fig. **154** Implementation of exercise training with pulse frequency adapted to age, using the step-climbing unit (without O_2 application: if possible 10—15 min daily). Climbing frequency selected so that the prescribed training pulse frequency is attained

exercise training adapted to his age [110]. If he fulfils this demand he can count on the measured improvement in his O_2 status remaining unchanged for months up to years. An energetic lifestyle, in the sense of our demand, exists when *regular physical exertion of the level seen from Fig.* **153** *takes place for 10 min daily*, analogous to the exercise training and with any types of exercise that come into consideration.

2.3.7 Exercise training must be fun

It has long been our experience that people only do things voluntarily for a long time that are enjoyable. Independent of the aspects of O_2MT already discussed, the following thoughts are therefore also of significance in the *individual designing of a permanently healthy and energetic lifestyle* under the conditions of our times. It was mentioned in the introduction to this book that lack of exercise is one of the greatest and still increasing dangers to human life in modern industrial states. The combat of this physical inactivity by means of suitable physical exertion, or the exercise training discussed, is therefore one of the medically most important demands of our days [266].

The American sports doctor and astronaut trainer Cooper even worked out a *score system* for the amount and control of the daily training, for certain exercise programs (running, swimming, cycling, walking, running on the spot, handball) [9]. The *exercise counter* shown in Fig. **155** allows one to check, to a certain extent, whether enough "exercise units" [9] have been performed daily. This counter represents a meaningful variation of the well-known step counters. It gives relatively characteristic guiding values, if carried in a vertical position as near as possible to the middle of the body, e.g. on the belt or dress.

The drug combination for the raising of the O_2 utilization, Fig. **126**, should always be taken before the daily exercise training in order to increase the effect [251].

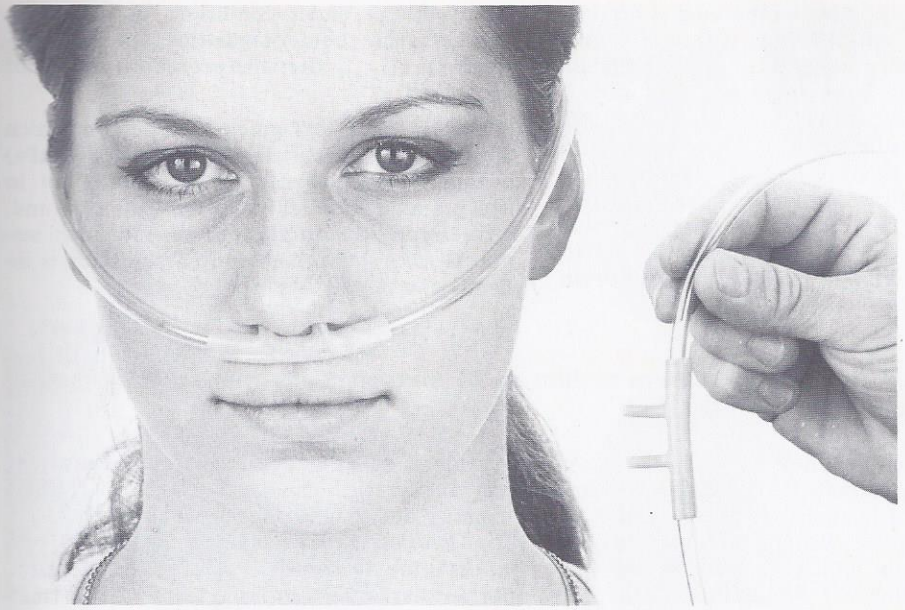


Fig. **163** O_2 nozzle applicator (open system), comfortable for user, therefore much used until 1982 despite great O_2 losses

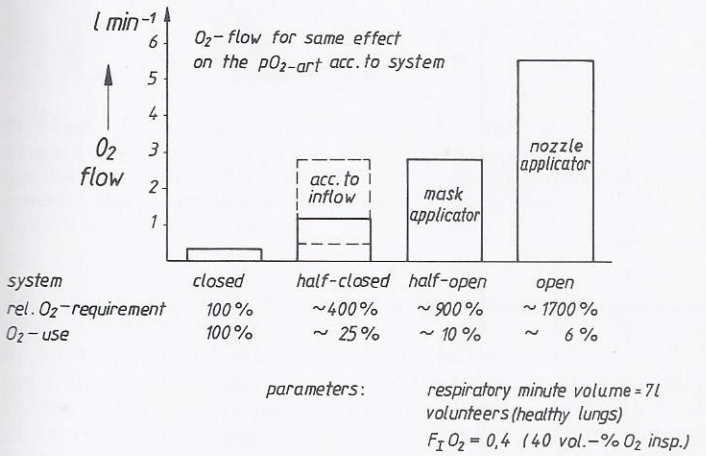


Fig. **164** O_2 flow for the 36 h O_2 O_2 multistep therapy process dependent on applicator system. The characteristic of the new soft plastic mask applicator is between the (previous) mask and nozzle applicator (relative O_2 requirement ~1360%; O_2 use ~8%)

requiring 10–20 times the O_2 flow needed in the closed system. There is a great "therapeutic range" in O_2 application. Therefore suffice it to give two limits, one corresponding to the minimum O_2 supply required for successful therapy, and the other corresponding to the maximum permissible amount (prevention of toxic side-effects in long-term application).

The lower limit in the 36 h O_2MT variant is a flow that will certainly bring about a $P_{O_{2\text{-art}}}$ of about 125 mmHg (16.6 kPa), so that the "switching threshold" for this procedure is reached or crossed.

The upper limit for the procedures lasting several hours is an O_2 concentration of 40 vol% O_2, which is generally accepted to be unproblematical, and which is achieved using a mask applicator with storage balloon with a mean flow of 3.5–4 l/min.

If too great an O_2 flow to the lung is brought about in the 36 h O_2MT procedure (at a normal RMV under resting conditions), e.g. by the use of a close-fitting mask applicator with storage balloon, the $P_{O_{2\text{-art}}}$ levels of, e.g. 250 mmHg (33 kPa) can result during the treatment. With such excessive levels a *gradual counter-regulation in the lung system* normally occurs, which in our example reduced the given starting value to 200 mmHg (26 kPa) after 20 min, and to 150 mmHg (20 kPa) after 40 min. It was often observed that under conditions of the occurrence of such counter-regulation, the lasting increase in $P_{O_{2\text{-art}}}$ after the procedure is only of a low level.

In the 15 min O_2MT quick procedure, in which the $P_{O_{2\text{-art}}}$ reaches levels of 350 mmHg (47 kPa) under an O_2 flow of, e.g. 30 l/min, but in which a high RMV exists at the same time and, furthermore, the duration of the individual session is only short, the counter-regulation is insignificant.

3.1.2 Practical aspects. Measurements confirm the O_2 mask applicator with storage balloon to be a good solution

In order to maintain the long-lasting improvement in the O_2 status after O_2MT, the O_2 flow must be selected in terms of the level and duration so that the "*switching threshold*" of the procedural variant used (which shows a not inconsiderable individual variation from person to person) is crossed. The fact that in the past some medical experts were repeatedly unable to confirm the lasting improvement in the O_2 status by means of O_2MT, or were not able to confirm it with the frequency found elsewhere, was due to this condition not being fulfilled – partly due to ignorance of its existence [17]). The *faultless implementation of the O_2 administration* is therefore one of the most important tasks in the practice of O_2MT treatment.

Instead of theoretical considerations of O_2 administration with the mainly used open and half-open systems, which had been made in the

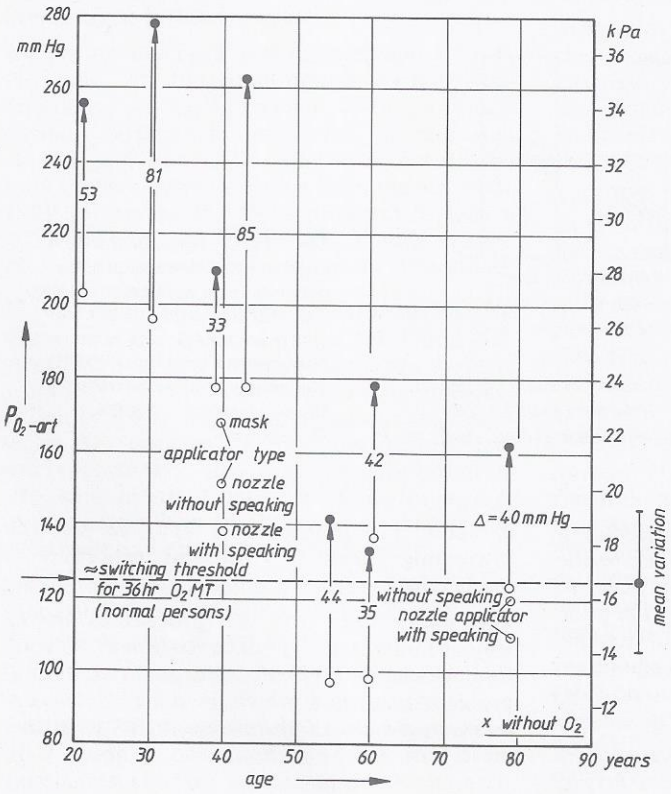


Fig. 165 Measurements of the arterial P_{O_2}, at rest, under an O_2 flow of 4 l/min through different applicators of soft synthetic material without and with storage balloon. Applicator quality: Mask applicator with storage balloon, very high; mask applicator without storage balloon, high; nozzle applicator, low

been accomplished when, at the end of the inhalation phase, the storage balloon has just been deflated. This simplifying procedure can be useful in order to save the costs of an O_2 flowmeter or the expensive technical equipment for physical exertion (bicycle ergometer, manual ergometer, rowing device, running belt etc.) in treatment in the patient's home.

3.1.3 Administration of oxygen in a closed room

The O_2 enrichment of the air of a whole rest room, in accordance with the variants shown in Fig. **168**, relieves the user of the necessity of wearing a more or less uncomfortable applicator. This significant advantage is opposed by several disadvantages, some of them serious: an augmented proportion of O_2 in the air in the vicinity of flammable objects means an increased risk of fire. The O_2 enrichment of the air of a whole room (Fig. **168** A) therefore demands a series of safety measures of unquestionable efficacy, the expense of which prohibits a broad application of this system from the start. Only relatively small working cabins or resting tents (Figs **168** B and C), in which the risk of fire is reduced due to a smaller volume, can be used in such a way as to fulfil fire precautions and aid the necessary measures within reasonable limits.

The required total amount Q_K of O_2-enriched air for maintaining an atmosphere having a constant oxygen content $\overset{+}{c}O_2$ in a cabin with the volume Q_O is composed of the

- flow of the feed-gas (F_{KA}) with the oxygen concentration $c_{O_2\,KA}$ and the
- initial filling volume to attain the desired oxygen level in the cabin by "rinsing" and "blowing".

Provided that the CO_2 is not absorbed by special devices, the requirements of O_2-enriched air during a treatment are primarily determined by the fact that, at the end of the session, the CO_2 concentration of the recycled air must not exceed the limit of $\leqslant 1\,\%$ despite the continuous generation by the experimental subject ($\approx 5\,\%\ CO_2$ in the expiration air). The diagrams in Fig. **169** give detailed information on the volume of O_2-enriched air thus required and also for the initial filling of the cabin. It can be seen that, for longer periods of administration, the amount of O_2-enriched air fed into the cabin must be approximately 4 (!) times greater than the volume needed by the individual because of the necessary removal of CO_2. On the other hand, short periods of application are uneconomical from the start, due to the large initial volumes for "charging" the treatment chambers, cabins or whatever.

An improvement of this unfavorable, O_2-wasting procedure could be attained by the reduc-

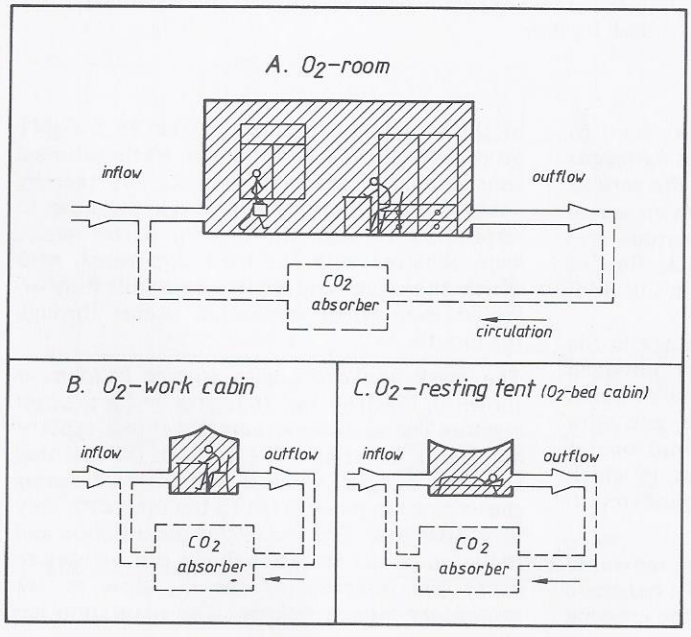


Fig. **168** The application of O_2 enriched air in rooms for different purposes

Fig. **170** Respiration mask, worn over the mouth and nose, with warmth-isolating terry-cloth cover for use in the O_2 multistep sauna. Construction type: Oxyparat Allihn, D-8000 Munich, FRG

3.1.4 Oxygen application for special conditions

O_2 applicators for use in the O_2MT sauna had to be developed bearing the high room temperatures in mind. Figures **170** and **171** show constructions with which burns due to contact with hot metallic parts etc. can be avoided.

With the construction shown in Fig. **171** an O_2-enriched zone is formed in front of the nose and mouth, from which the person breaths the desired gas mixture.

In order to keep O_2 losses at a low level, it is not only necessary to optimize, as discussed the O_2 inlet as such, but also to adapt the supply of O_2 to the respiratory process itself. Theoretically, there is a slight loss of this type if the O_2 supply only occurs in the immediate phase of inhalation, when a high rate of influx exists. Measurements using impedance plethysmography, as in Fig. **172**, showed that the favorable interval of the respiration phase amounts to roughly 30% of the total time needed for inhalation and exhalation (duration of respiratory period).

Respiratory phase switches, controlled electronically by a thermistor, have not yet been able to take the place of the much simpler *O_2-saving storage balloon*. They were complicated and expensive. The respiratory phase switch, controlled *thermally* by the respiratory gas flow, is much simpler in its design and effect and is, in the design shown in Fig. **173**, combined with the O_2 mask applicator. This kit was put on the market early in 1986 by Allihn, Munich, FRG. There is a 50% saving of oxygen compared with the mask applicator without storage balloon.

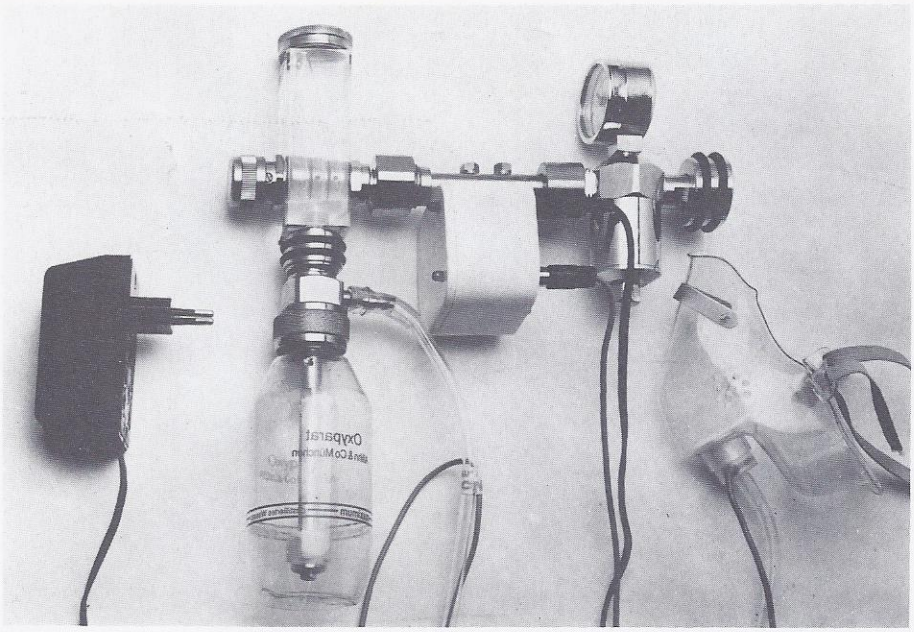


Fig. **173** Respiratory phase switch, thermo-controlled by the respiratory gas flow (Manufacturer: Allihn & Co., D-8000 Munich 70, FRG)

3.1.5 Hyperbaric oxygen therapy and hyperbaric O_2MT. Most intensive variants

The oxygen therapy using a hyperbaric chamber [274, 275] and the O_2MT do not oppose each other; rather, they should be seen as variants closely bound together and complementing each other. This complementation refers mainly to important fields of application where the higher O_2 pressure brings about greater or faster effects, which do not occur in the normobaric O_2MT (e.g. combat of anaerobic infections such as gas gangraene, tetanus, or treatment of acute hearing loss etc.). From the point of view of O_2MT it virtually goes without saying that in treatment in the hyperbaric O_2 chamber the discovered capillary wall switching mechanism of the blood microcirculation (see Paragraph 1.1.1) is often, or even usually, triggered in a positive direction which lastingly improves the O_2 status. The occurrence of this "high-charging" and thereby existence of a real methodological relationship are also made probably by the fact that the same indications are given for the hyperbaric oxygen therapy (with the exceptions named), as were derived from the results of many tens of thousands of treatments with O_2MT. The following indications for hyperbaric oxygen treatments were given as early as 1968 [274, 275, 275a]:

Neurology:
Stroke and its late effects
Prognosis of a successful, extraintracranial bypass operation
Cerebral circulatory disorders

ENT:
Sudden loss of hearing
Tinnitus

Surgery, angiology:
Chronic ulcera cruris
Skin transplantation
Arteriovenous occlusive disease

Further indications:
Multiple sclerosis
Spinal cord injury
CO poisoning
Cyanide poisoning
Ergot poisoning
Osteoradionecrosis
Chronic osteomyelitis
Crush injury
Compression syndrome
Actinomycosis
Burns
Cerebral hypoxia after attempted suicide by strangulation

Therapy-resistant ventricular and duodenal ulcers
Malignant otitis externa
Hardness of hearing due to noise
Peripheral circulatory disorders

The extent of the increase in the resting $P_{O_{2\text{-ven}}}$ during the different treatment variants with hyperbaric oxygen has not yet been investigated. There is also a lack of published results on the lasting improvements in the O_2 status after treatment. Since very high levels of the $P_{O_{2\text{-art}}}$ (850–1140 mmHg, corresponding to 113–152 kPa) were detected during hyperbaric oxygen treatments [276], we can be sure that, in accordance with Fig. 3, P_{O_2} levels $\geq$ 50 mmHg (8 kPa) exist at the venous end of the capillaries without physical exertion. With the named P_{O_2} pressures and the usual management, with, e.g. 20 sessions of 90 min duration in the chamber, the triggering of the switching process must occur as in the 36 h O_2MT procedure (without significant physical exertion), and thus also the long-lasting effect. In order to *intensify the effects of the hyperbaric oxygen therapy* it is obvious that the 1st and the 3rd step of the O_2MT should also be applied. This thought leads us to the interesting concept of the *hyperbaric oxygen multistep therapy* with additional increase of the $P_{O_{2\text{-ven}}}$ under O_2 excess by means of raising the capillary blood flow $\dot{Q}$ by strong physical exertion. The reader should remember here the relation to the strength of the effect of the O_2MT procedures, shown in Paragraph 1.1.1.2. In treatments in the high-pressure chamber, too, this measure for the raising of the $P_{O_{2\text{-ven}}}$ during the treatment (by means of physical exertion) should not be omitted if at all possible (increase in the effect and reduction in duration of the procedure). A scientific investigation into the specific effects of the hyperbaric oxygen multistep therapy is at present being carried out by B. Fischer (see below).

The effort involved in the hyperbaric oxygen multistep therapy is unquestionably justified in the treatment of particularly severe cases and in cases in which an additional pharmacodynamic effect of the oxygen should be exploited ($P_{O_{2\text{-art}}} > 100$ mmHg $\triangleq$ 130 kPa).

Peripheral circulatory disorders of the lower extremities in diabetics, which have reached the stage where amputation is becoming necessary, are an example of this. In such situations we must use all means to combat the peripheral circulatory disorders. In the normobaric O_2MT we had therefore recommended the inclusion of the HOT* treatment and, if necessary, hemodilution in such cases [74]. The chances of success seem much better even than this using the hyperbaric oxygen multistep therapy, if necessary again with the further complementary steps of HOT* and hemodilution. For both hyperbaric and normobaric O_2MT a normal hematocrit is an absolute prerequisite. If it is higher than normal, it should be reduced to at least 45 %. A study of therapeutic limits of such intensive variants should soon be carried out with patients who have reached the critical stage discussed.

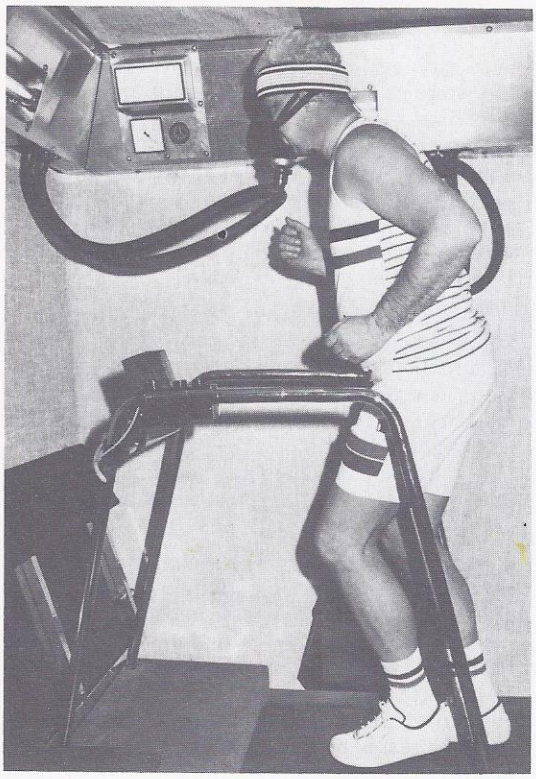
Recently the term HBO (hyperbaric oxygenation) has been used increasingly and internationally for hyperbaric medicine, and in many countries there are numerous systems for it, starting from one-person chambers up to large high-pressure chambers for the simultaneous treatment of several persons (up to ten patients and more) at pressures up to 10 bar and more ($\triangleq$ 1 MPa).

An exemplary high-pressure chamber has been in use in the Fachklinik Klausenbach für Frühgeriatrie der LVA in Nordrach-Klausenbach, FRG, since the early 80s. Senior Consultant Prof. Dr B. Fischer has performed well over 10 000 treatments without complications and has gained particularly good results in the combat of diseases of the inner ear (sudden loss of hearing, deafness due to explosions etc.) and in the treatment of cerebral insufficiencies. An exchange of experiences has been going on for a good year.

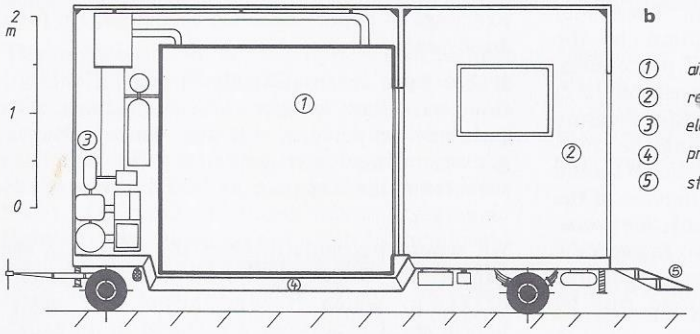
It has been internationally shown in the last few years that, with various indications, it is possible to perform therapy more advantageously using lower pressures than had been seen from the experiences of submarine medicine.

We would particularly refer the reader to the papers by Holbach, Caroli and Wassmann [277], in which it was shown that better neurological results were attained at an excess pressure of 0.5 bar (50 kPa) than at double the level.

Lower levels of high pressure make possible a simpler type of construction for the chambers, and it is even possible to use these simpler systems mobilely. Erwin Braun in Engelberg, Switzerland, designed and produced a mobile high-pressure chamber with a maximum operational pressure of 1.25 bar (125 kPa), in which up to nine persons at a time can sit and undergo therapy. Figure **174** shows a side view of this mobile system, presented in Basle in February 1986, and also shows how a running-belt is mounted in this chamber to enable precise ergometry, on which a volunteer exercises, connected to the O_2 supply.



a



b

① airtight chamber
② rest room
③ electrical equipment
④ profile aluminum chassis
⑤ steps

Fig. 174 Mobile hyperbaric O_2 chamber (up to 1.25 bar) according to Erwin Braun, Engelberg, Switzerland. Inside view
a) Inside view with running belt for exertion
b) Scheme of layout

The development of mobile high-pressure chambers of this type makes possible the necessary extension of the basis for clinical research with HBO, and we regard this as being so important that we have ordered one of the first chambers of this type and want to make it available to the external branch of our Institute at the nearby Weisser Hirsch clinic.

It should also be noted that the pressure-equivalent "effective diving depth" lies at 10 m and below. That means that the "zero time" lies in the normal therapeutic times and that it is always possible "to surface" at short notice. There is no longer any need for a decompression department.

30 feet is 1 atsmosphere (ATMs)
Hard chambers provide up to 3 ATMs
there for up to 90% O2 over soft chambers

3.2 Technology of the provision of air mixtures with increased P_{O_2}

3.2.1 Oxygen requirements in the various procedures of the O_2MT

The additional O_2 requirements of the organism under the various variants of the O_2MT at physical rest and in physical exertion is a decisive value for the calculation of the systems for O_2 provision necessary for therapy. This value determines the *time of provision* for oxygen from a store (pressure cylinders, Dewar vessels with liquid oxygen), and in devices for continual O_2 supply it determines the *dimensions of the O_2 production performance* of the device.

The values of the *oxygen flow rates $\dot{Q}_{O_2}$ in the most important procedures of the O_2MT* are to be taken from Fig. **175**. In the interests of a good procedural effect, it must always be ensured that a *flow rate of the respiratory gas $\dot{Q} = \dot{Q}_{O_2} + \dot{Q}_{N_2}$ is adaptable of the prevailing level of the respiratory minute volume (RMV)*. For the adjustment and control of the supply of respiratory gas or additional O_2 to the applicator, gas flow meters (rotameter principle, cf. Fig. **171**, left, or with analogue display) with different measuring ranges are necessary. These flowmeters are often combined with an additional fine valve and also with a gas humidifier.

In the O_2MT quick procedure (variant GK 2), in which the RMV is multiplied as a result of the high level of physical exercise, the O_2 flow rate is also multiplied, as can be seen from Fig. **175**. (Although the 15 min O_2MT quick procedure works with virtually pure oxygen,

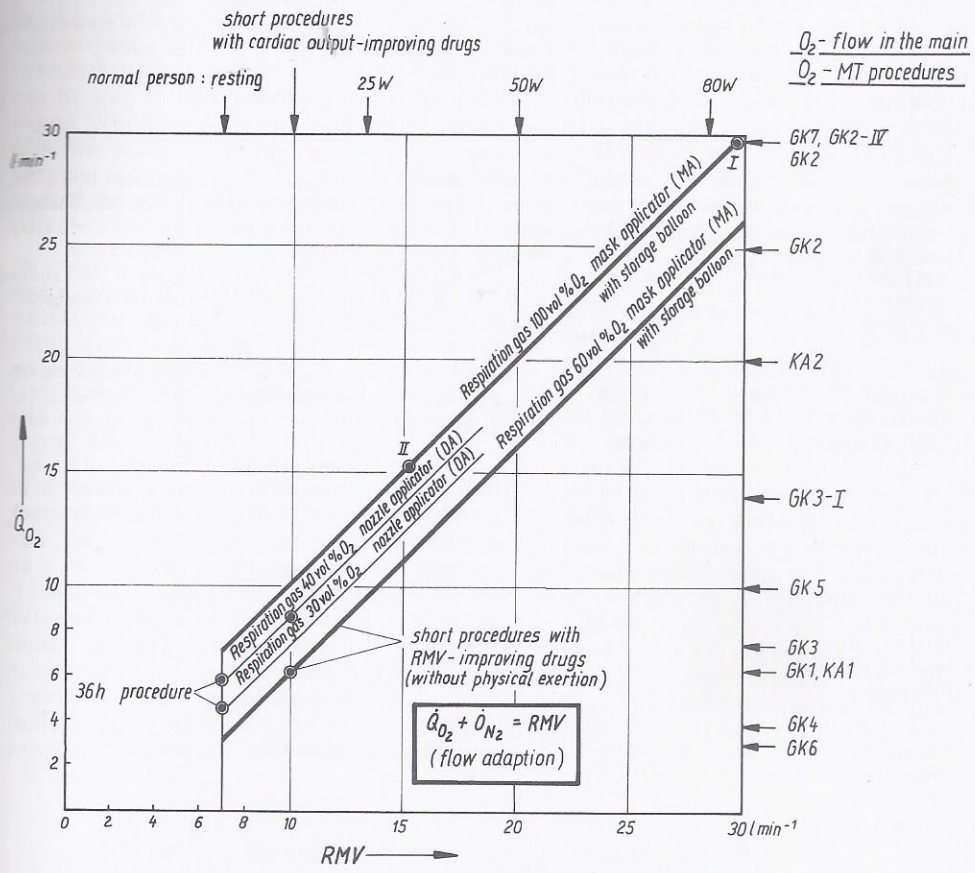


Fig. **175** Oxygen flow rate $\dot{Q}_{O_2}$ in the main O_2MT procedures. Mask applicator with storage balloon (semi-open system)

and although the flow rate for this variant is between 25 and 30 l/min, the O_2 requirement for the whole procedure is reduced to roughly 5–10 % of that for the 36 h procedure, because the duration of the quick procedure is only 1–3 x 15 min.

For non-able-bodied or disabled persons, for whom it is not possible to raise the cardiac output by physical exertion, we tried to reduce the duration of the procedure by the administration of drugs, which increase the cardiac output and RMV for some hours, even at physical rest.

Table **18** O_2 supply from stores [279–284]

Method	Work principle	O_2 content	Content (volume)	O_2 supply output l/min	O_2 supply volume (normobaric)	Area of use	References (remarks)
1 Pressure cylinders	1.1 Filled in special works for technical gases (transportation increasingly awkward above 20 l cylinders)		0.8 l	variable	160 l	outpatient	steel light weight cylinder (200 at) in carrying bag
			2 l	dto.	400 l	also outpatient	280
		≈ 99	10 l	dto.	2000 l	at home	(steel cylinder 150 at)
			20 l	dto.	3000 l	stationary central supply units	(steel cylinder 150 at)
			40 l	dto.	6000 l		
2 Central supply units	2.1 Supply at reduced pressure from batteries of 40 pressure cylinders (laborious)	≈ 99 (pressure in pipe 5 at)	larger number 40 l cylind. e.g. 2·10	4–16 per single delivery	60 000 l in use in reserve	in larger clinics central supply units	278, 280 (centre conveniently located)
	2.2 Supply from liquid oxygen, using a transportable cryotank with e.g. 100 l contents (pressurized gas producer)	≈ 99 (pressure in pipe 5 at)	several tanks (10^4 l liquid O_2)	4–16 per single delivery	80 000 l per tank, storage time 85 hrs ($8 \cdot 10^6$ l)	in larger clinics central supply units	280, 281 Linde AG, Tech. gases, D-8023 Höllriegelskreuth (care in the handling of liquid oxygen) 282
3. Generation by decomposition of oxygen-rich chemicals	3.1 Reaction: $NaClO_3+Fe \rightarrow NaCl+FeO+O_2$	60	equipment mass 2.5 kg (0.88 kg $NaClO_3$)	3	180 (2x90) two charges	outpatient very easy to transport	283 Med-ox-equipment from Scott-Aviation, Lancester, N.Y., USA (two charges, which can be discharged in sequence or parallel)
	3.2 Reaction: $2H_2O_2 \rightarrow 2H_2O+O_2$ (catalyst) H_2O_2 as 30% aqueous solution; Perhydrol)	99	(2 kg Perhydrol)	3	200	outpatient	284 (Japanese small-sized equipment 1970)
	3.3 Reaction: $2Na_2O_2 \rightarrow 2Na_2O+O_2$ (catalyst or heat)	99	(2 kg Na_2O_2)	3	285	outpatient	284
	3.4 Decomposition, e.g. of $KMnO_4$ at T > 200 °C	99	(1 kg $KMnO_4$)	3 (after heating-up time)	142	outpatient	283 (mains-operated heating)

3.2.2 The various types of oxygen provision

The technology for the *provision of additional oxygen* at rates of 1.5–5 l/min for a few or for many hours, or at rates of 5–50 l/min for durations of a few hours to a few tens of minutes, has entered a new phase. The most recent developments in the various branches of this specialist technology all have the common characteristic that the O_2 can be delivered to the sick or healthy person in a much more comfortable way than ever before [278]. The needs of patients with certain lung disease, and of asthmathics, can be seen to have contributed just as much to this development as the effort periodically to counteract the increasing air pollution in conurbations of cities. For the O_2MT this development leads to the fulfilment of the essential technical preconditions in order to enable this therapy to be applied on a broader basis even in smaller clinics, outpatient clinics, medical practices, sanatoria, as well as in the home.

In the systems for *O_2 provision from stores*, summarized in Table **18**, *lightweight steel cylinders with a capacity of 160–400 l O_2* can be seen to be advancing in the field of individual requirements. For outpatient application, the production of units with a capacity of between approximately 150 and 300 l has been started, in which O_2 is generated by the decomposition of oxygen-rich chemicals.

In central O_2 supply, the *provision from batteries of 40 l pressure cylinders* (e.g. from Allihn, Munich, FRG, or Weinmann, Hamburg, FRG) and from *liquid oxygen tanks or pressurized gas producers* is being accomplished in larger clinics [282]; cf. especially the production programmes of Linde, Höllriegelskreuth, FRG.

In the system for *O_2 provision from continual production*, which is summarized in Tables **19** and **20**, very recent technical developments have caused a new situation to arise. Until now there were virtually only the extensive systems of cryogenic engineering [280, 281] to produce liquid oxygen. The relatively high production performance of systems which are so extravagant in terms of equipment and servicing, limits their application to the direct or indirect supply of large clinics. With the creation of systems for *O_2 separation with zeolite molecular sieves* [285, 286], *a relative easy provision of O_2 is opened up for application in the home*. A new branch of the medical industry could be in the making. Even *O_2 separation with membrane systems* [287], which is still at a very stage, has already led to experimental set-ups with interesting features [288], cf. Table **20**, column 2.1.

It is a fascinating aim of further research on the theme of this book so to develop further the membrane systems for selective gas permeation, that the pressure difference occuring in normal breathing is enough to cause sufficient O_2 provision. Elements which could be helpful in the development of highly selective membranes (under investigation) are indicated in column 2.3 in Table **20** [289]. In the performance of this task a type of O_2 mask would result which would be able to help patients with critically reduced cardiopulmonal performance, up to the total duration of the daily cycle. That such an O_2 mask, which with a light construction could be conveniently carried with the patient in a shoulder bag, could, for example, in persons with advanced lung insufficiency (for whom the O_2MT does not usually work), permanently produce the same strength of O_2 supply to their tissue as existed in younger years is a thought that spurs us on to intensive action.

In the course of our continuous efforts since 1969 to discover technically and economically practicable methods of O_2 provision with rates between 1.5 and 10 l/min, models were built, or experimental investigations performed into the generation of O_2 by *electrolysis of water*, by *oxygen ionic conduction in solid state electrolytes*, by the *reversible complexing of O_2 to an desorption from organic Co-complexes (salcomin)*, by utilizing *the different gas solubilities in liquids*, and by means of *green algae*. These studies form the basis of the data and assessments given in Table **20**. None of these five methods has as yet led to more favorable results than O_2 separation with zeolite systeme (and with membranes). For this reason we only deal with the technical realization of these two main methods later in this chapter.

Table 19 O_2 provision from continuous production, zeolite systems [285–288], prospective solution

Method	Working principle		O_2 concentration vol.%	Size h, w, d (cm) Mass (kg)	O_2 provision O_2 addition (l/min)	O_2 mix l/min	Area of use	Remarks
Separation by zeolite systems	Selective adsorption of N_2 to specific zeolites	1.1 Pressure swing at excess pressure (250 kPa)	55 to 93	75x30x75 / 60	4.3 4.85 5.16 4.55	10 (55 vol.%) 8 (69 vol.%) 6 (89 vol.%) 5 (93 vol.%)	at home, in clinics without central O_2 supply, for O_2MT variants GK4, GK6; mobile unit on castors, noise level 48 dBA, N=0.4 kW	O_2 selector and additional reservoirs Development IvA, Dresden, GDR Performance adapted
		2-step cycle			—	—		
		1.1.1 Additional O_2 reservoir 1	93	0.5 m^3	Storage 450 l (standard)		additional unit at 1.1 for quick procedure GK2, GK2-II, GK2-III	performance adapted to all O_2MT variants
		1.1.2 Additional O_2 reservoir 2	93		Storage 3500 l (special supplement)		additional unit at 1.1 for 120–60 min obstetrics procedure GK2-IV	large series production Hauni-Werke Körber, Hamburg, FRG (1986)
		1.3 Pressure swing at excess pressure	60 to 92	72x30x57 / 37	2.0 2.3 1.8	4 (60 vol.%) 3 (80 vol.%) 2 (92 vol.%)	at home for long-term therapy with low O_2 flow mobile unit on castors, noise level 50 dBA, N) 0.28 kW	Permox development and production Dräger-Werk, Lübeck, FRG (1982)
		2-step cycle						
		1.4 Pressure swing at excess pressure	60 to 95	58x44x41 / 38	2.0 2.3 1.9	4 (60 vol.%) 3 (80 vol.%) 2 (95 vol.%)	at home for long-term therapy with low O_2 flow mobile unit N) 0.28 kW	"Oxymat" development and production Weinmann, Hamburg, FRG (1985)
		2-step cycle						
		1.5 Pressure swing at excess pressure	60 to 96	71x53x37 / 44.5	3.0 2.6 1.9 1.0	4 (80 vol.%) 3 (89 vol.%) 2 (94 vol.%) 1 (96 vol.%)	at home for long-term therapy with low O_2 flow mobile unit on castors, noise level 45 dBA, N = 0.35 kW	"Med-O_2" development and production Buderus, Wetzlar, FRG (1985)
		2-step cycle						
		1.6 Pressure swing at excess pressure	60 to 90	adapted to local conditions	200 — 100	400 (60 vol.%) — 120 (90 vol.%)	larger cure centers, smaller clinics, intensive care	large O_2 selector, development IvA, Dresden, GDR (1984)
		2-step cycle			O_2 flow also sufficient for GK2, GK5 and GK7 variants			

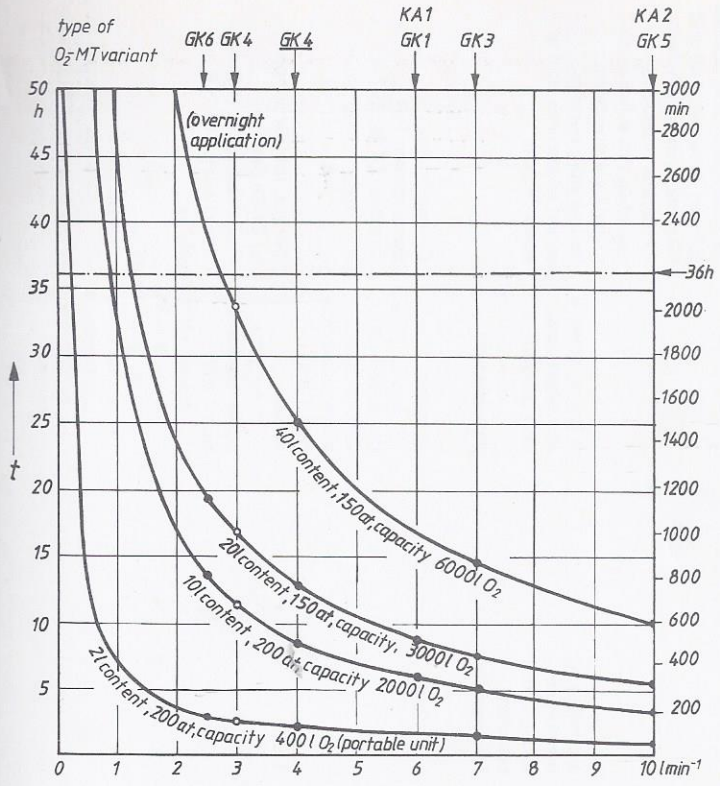


Fig. **176** O_2 delivery capacity of various standard-sized O_2 pressure cylinders expressed as the time t during which a certain O_2 flow $\dot{Q}_{O_2}$ can be maintained. On the upper abscissa the O_2 demand of some O_2MT variants is indicated

3.2.3 Oxygen provision from pressure cylinders

The volume and capacity of the various standard types of O_2 pressure cylinders have already been given (cf. Table **18**). With the development of the O_2MT quick procedure and the O_2MT short procedure, O_2 provision from pressure cylinders has gained importance for two reasons:

1. because the total amount of O_2 required per procedure has become much smaller, compared with the 36 h O_2MT variant, and
2. because the higher O_2 flow rate necessary for the new short versions of the O_2MT still exceeds the separation efficiency of the zeolite selectors available at present.

For how long one can manage on a certain type of *oxygen cylinders* in dependence on the flow rates needed for the common O_2MT procedures is to be taken from Figs **176** and **177**. For the requirement of the 15 min O_2MT procedure the contents of 2 l bottles are sufficient, as can be seen, for which a convenient portable unit is available. For outpatient use, the contents of one 2 l light-weight steel cylinder, which can be easily transported in a carrier bag, are often enough.

As soon as we are no longer dealing with individuals, but with larger numbers of patients, the use of large, difficult-to-transport pressure cylinders cannot be avoided. In cure institutions it has proved worthwhile to install a *row of 40 l cylinders* (filling pressure 150 at, 6000 l O_2 capacity per cylinder), with pressure-reducing valve and in observation of safety regulations, in a fixed position immediately next to access for lorries. From this place the oxygen is led to the individual treatment rooms with their O_2 taps via low-pressure pipes. Each *O_2 unit* combines a *Rossignol valve*, an *O_2 flowmeter* (e.g. rotameter), an *air humidifier* and a *mask applicator of flexible plastic material*.

Complete sets of this type can be obtained from e.g. MLW (Leipzig, GDR), EMC (Aachen, FRG), Allihn (Munich, FRG), Eumatron (Munich, FRG), Weinmann (Hamburg, FRG), SMT-Geräte-Vertrieb (Berlin West), Linde (Höll-

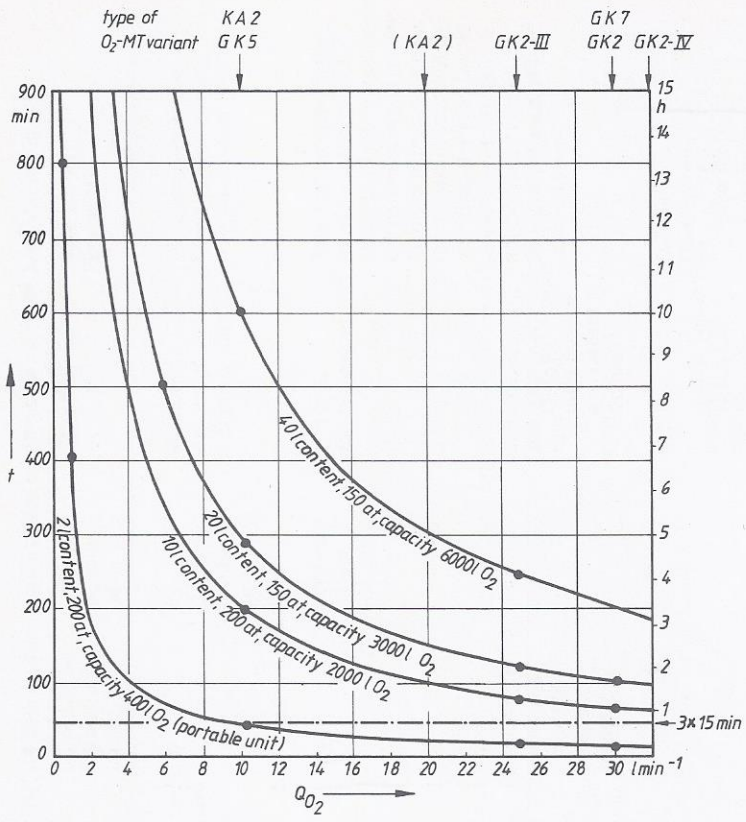


Fig. **177** O_2 delivery capacity of various standard-sized O_2 pressure cylinders expressed as the time t during which a certain O_2 flow $\dot{Q}_{O_2}$ can be maintained. On the upper abscissa the O_2 demand of further O_2MT variants is indicated (cf. Fig. **176**)

riegelskreuth, FRG), and Draeger (Lübeck, FRG). Since the difficulties in obtaining workers to transport large steel cylinders are constantly increasing, the development of the devices described in the following two paragraphs for deployment also in cure institutions and clinics should be warmly welcomed, provided that their performance is sufficient to deliver the O_2 flow for the intended O_2MT procedures.

3.2.4 Oxygen provision from zeolite separators

O_2 provision from zeolite devices is at present the most developed of the systems given in Tables **19** and **20**. The *"O_2 Selector"*, which was developed in 1973 in our Institute and has since then been tested medically, should be named here. This historical device, which is characterized by an alternating operation between two cylinders and a pressure swing between atmospheric pressure (adsorption) and reduced pressure (desorption), is shown in Fig. **179**.

The data given in Table **19** show that this apparatus is just in the position to supply the O_2 flow named in Paragraph 3.1 (recently established to somewhat higher), for both the 36 h and the 15 min O_2MT procedure. It is of great practical significance that this device, with its O_2 output adapted to all variants of the O_2MT, will be put on the market in 1988 by *Hauni-Werke* (Hamburg, FRG) in a large series of 10 000 and at a reduced price thanks to support from the Kurt Körber Foundation (cf. Fig. **180**).

The O_2 generation of the less efficient devices usual today is *not* sufficient. This should not surprise us, as the smaller devices were created for a different purpose, namely for long-term therapy in the home, where a smaller O_2 flow is adequate. The firms DeVilbis (USA), Draeger (Lübeck, FRG), Weinmann (Hamburg, FRG)

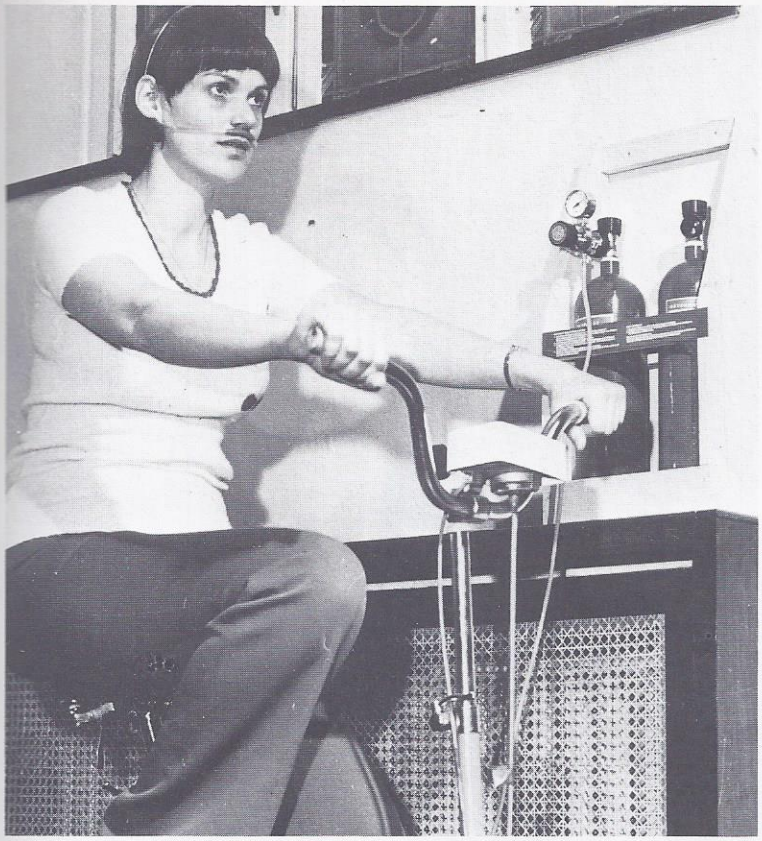


Fig. **178** 2x2 l light steel pressure cylinder unit providing 800 l O_2 (Oxyparat Allihn, Munich, FRG) in the application of O_2MT with bicycle ergometer

etc. also brought out small devices around 1982, and Buderus (FRG) in 1985.

The following lines should give some details for the orientation of the reader on the *technical solution of the Dresden "O_2 Selector"*, especially designed for the requirements of the O_2MT. The device supplies in 22 h in its product gas the same amount of additional oxygen as is contained in a 40 l (150 at) pressure cylinder, For gas separation this device applies the principle of selective and reversible nitrogen adsorption on special zeolites (molecular sieves). It uses the zeolite type KX and, recently a fine-pore type from the Elektrochemisches Kombinat (Bitterfeld, GDR). The atmospheric nitrogen is adsorbed and desorbed by changing the pressure. In the adsorption phase O_2-enriched air remains as the product gas of the device [286, 295]. The "O_2 Selector" contains two vessels filled with zeolite, which are cyclically and sequentially evacuated, flooded and rinsed.

The speed with which the steel cylinder will be partially replaced by zeolite devices or analogous systems in the envisaged medical and therapeutic facilities, will depend on the price, i.e. therefore also very much on the scale of their production. As far as their technology is concerned, they do not need to cost much more than household devices of similar size, washing machines for example.

The precondition for a transitions of the O_2MT into broad use in medicine and the health service is a low price for devices which can provide oxygen at a flow of 5 l/min and which can be equipped with economical storage accessories for, e.g. 30 x 15 = 450 l O_2 (filling time 1.5 h; sufficient for the 15 min O_2MT quick procedure). A low price will make possible the utilization of this universal therapy for poorer sections of the population, for procedural repetitions in the home, for places without O_2 provision from pressure cylinders, and for doctors and patients in developing countries. Thus the decision of Dr Kurt Körber, already mentioned, to produce 10 000 devices of this type in the Hauni-Werke (Hamburg, FRG) subsidized from the means of the Körber

Fig. **179** The first GDR zeolite operating O_2 selector device, developed in the Manfred von Ardenne Research Institute, Dresden, GDR, 1973. Maximal O_2 provision 5 l/min at an enrichment factor of 60 vol.%. This prototype has been further developed according to Table **19** in order to meet the grown O_2 demand of the different O_2MT variants. As mentioned in the text, the new version having a 450 l storage unit is manufactured at a large scale in the Hauni-Werke, D-2050 Hamburg-Bergedorf, FRG

Foundation, has opened the door to *new ways of helping people against many diseases, problems and complaints, and to ways which often prevent illness by the prompt elimination of their cause* (energy deficiency).

It is possible that the conditions for the development of economical and smaller devices for O_2 provision will improve even further in the next ten years. It has already been possible to *perfect the separating properties of the zeolite molecular sieves by doping (e.g. with ZnO, SnO_2 etc.) and also O_2-selective membranes, discussed in the next paragraph, by coatings of the most varied kinds* (Fraunhofer Institut, Stuttgart, FRG; Toshiba, Japan; Matsushita Electric Industry, Japan). Zeolite separators, fed with O_2-enriched air coming from preset O_2-selective membranes of high performance, are also already under discussion in order to improve yield and flow rate.

3.2.5 Oxygen provision from membrane filter devices

The process of *O_2 separation by means of selective permeation* through thin membranes seems in principle to be simple, and requires little energy. Research encountered difficult technological problems, however, since the necessary permeation rates can only be achieved using a relative large area of exceptionally thin membranes. For this reason a commercial

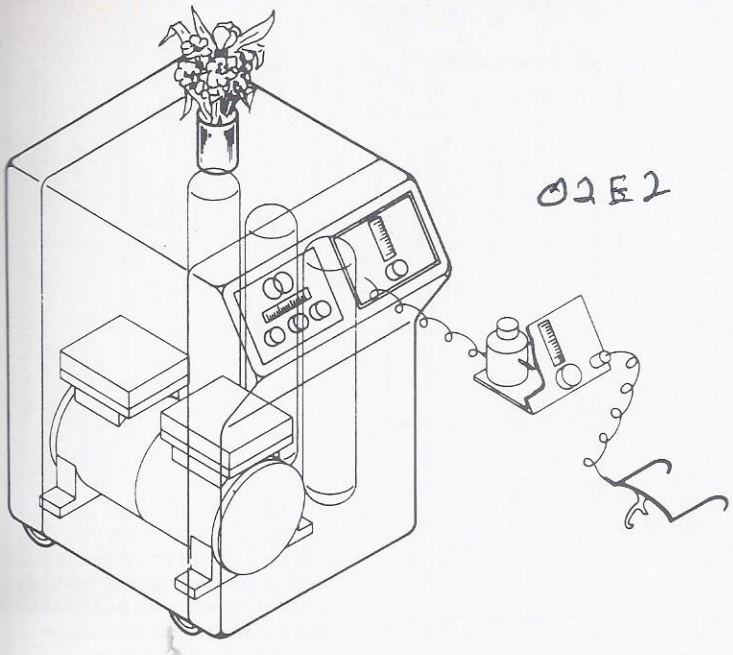


Fig. **180** Diagram of the O_2 selector basic device with O_2 provision adapted to the O_2 requirements of most O_2MT variants. Development: HAUNI-Werke, Hamburg-Bergedorf (FRG) in co-operation with the M. v. Ardenne Research Institute Dresden, GDR (5 l/min oxygen; weight ca. 40 kg; height x breadth x depth: 70 cm x 45 cm x 50 cm); large-scale production 1988

device [290], the data of which were given in Table **20**, column 2.1, is as yet only in its preliminary stages. Nevertheless the state of the developments leads us to assume that the process has a promising future.

The *principle* of the membrane filter process is shown in Fig. **181**. The initial gas mixture, normal air, passes over the membrane and leaves room 1 as O_2-deprived air, whilst in room 2, on the other side of the membrane, O_2-enriched air can be withdrawn. In order for this to function, a pressure gradient ($p_1 > p_2$) must exist above the membrane. In order to achieve this, either the feeding air is compressed, or the product gas is sucked off. The permeation through the membrane is determined by the properties of the material and is different for each gas component. For the component i, the permeation coefficient amounts to

$$Pr_i = \frac{\varphi_i \cdot x}{A \cdot \Delta p}$$

in which

- φ_i represents the flow of the component i through the membrane (permeating volume per time unit, corrected to standard conditions in terms of p and T),
- x the membrane thickness,
- A the membrane area, and
- Δp the pressure difference above the membrane.

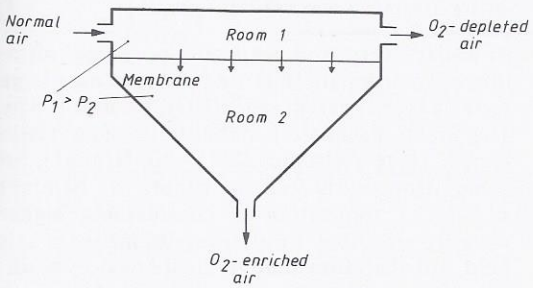


Fig. **181** Principle of O_2 enrichment with selectively permeable membranes

A series of materials, e.g. silicon rubber and organic polycarbonates, are of particular interest for O_2 separation by means of a membrane.

Silicon rubber has a large permeation coefficient of $Pr_{O_2} = 1.28 \cdot 10^{-11}$ cm²/Pa·s, but the separation factor is small: $Pr_{O_2}/Pr_{N_2} = 2.2$.

Polycarbonates, however, have a permeation coefficient of $Pr_{O_2} = 3.75 \cdot 10^{-13}$ cm²/Pa·s, but makes up for that by a separation factor of $Pr_{O_2}/Pr_{N_2} = 4.8$.

For a given flow φ_i, with a given thickness x and a given pressure difference Δp, the size of the permeation coefficient Pr determines the membrane area A required; the larger Pr is, the

3.4 Technology of the measurement of P_{O_2} in living tissues and in blood

3.4.1 Problems of P_{O_2} measurement in living tissues

The absolute value of the gain which occurs for tissue of the living organism during the O_2MT and its individual steps was originally assessed from the increase in the concentration of the energy-rich phosphate in the brain, i.e. from the increase in the O_2 metabolism in animals [4, 242], cf. Fig. **133**. This integral method is unsuitable for use in humans due to the necessary chemical processing of tissue samples. For humans we can use the method of direct P_{O_2} measurement in living tissue, which has been greatly improved in recent years [162, 166, 169, 272, 299–307], in order to perform quantitative studies. *The problem of P_{O_2} measurement with microelectrodes in the intercapillary space of living tissue* is presented in Fig. **192** and further commented on in Table **22**. According to the chance location of the insertion of a microelectrode with a sensitive tip of only a few µm (e.g. closer to the arterial or venous end of a nutritive capillary, or at a greater or lesser distance from the capillaries), different P_{O_2} levels, and also different ΔP_{O_2} levels will be measured.

Therefore the results of single *small-area measurements* only usually permit conclusions of a relative character. However, a large number of small-area measurements gives us a quantitative base for the frequency distribution of the P_{O_2} levels in the intercapillary space (Table **22**, column 1.1.2), a result of great significance. Such measurements are complicated and time consuming, however, which makes them only acceptable for research. The *large-area measurement* of the tissue P_{O_2}, which can be carried out with less effort, should therefore be preferred when the aim is to gain guidelines as to P_{O_2} profiles in living tissue (diagnosis) and as to the effects of measures taken (therapy).

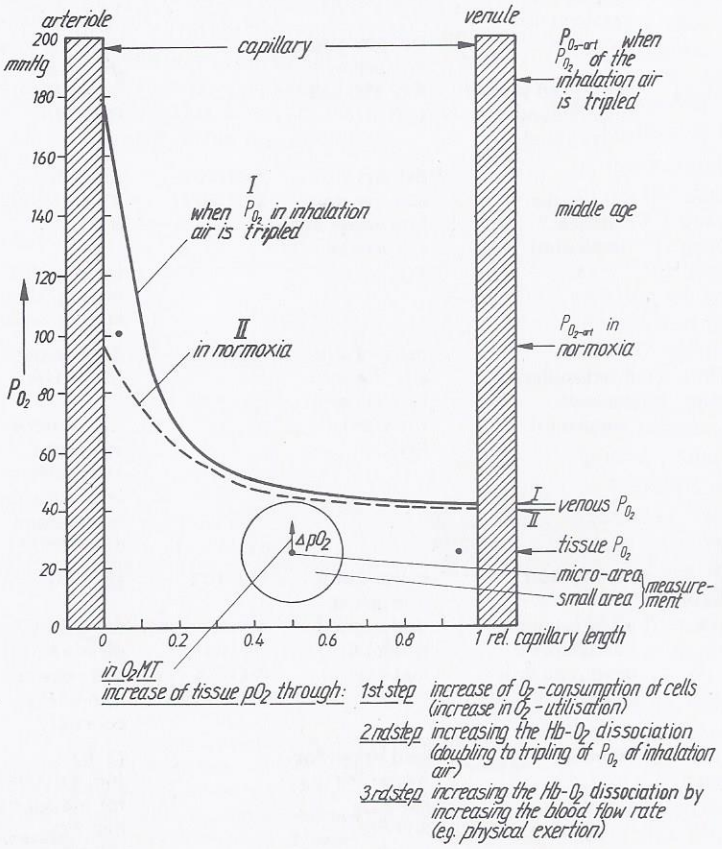


Fig. **192** Problems of micro-area or small-area P_{O_2} measurement in tissue between the arterial and venous ends of the supplying capillary (see also Fig. **97**)

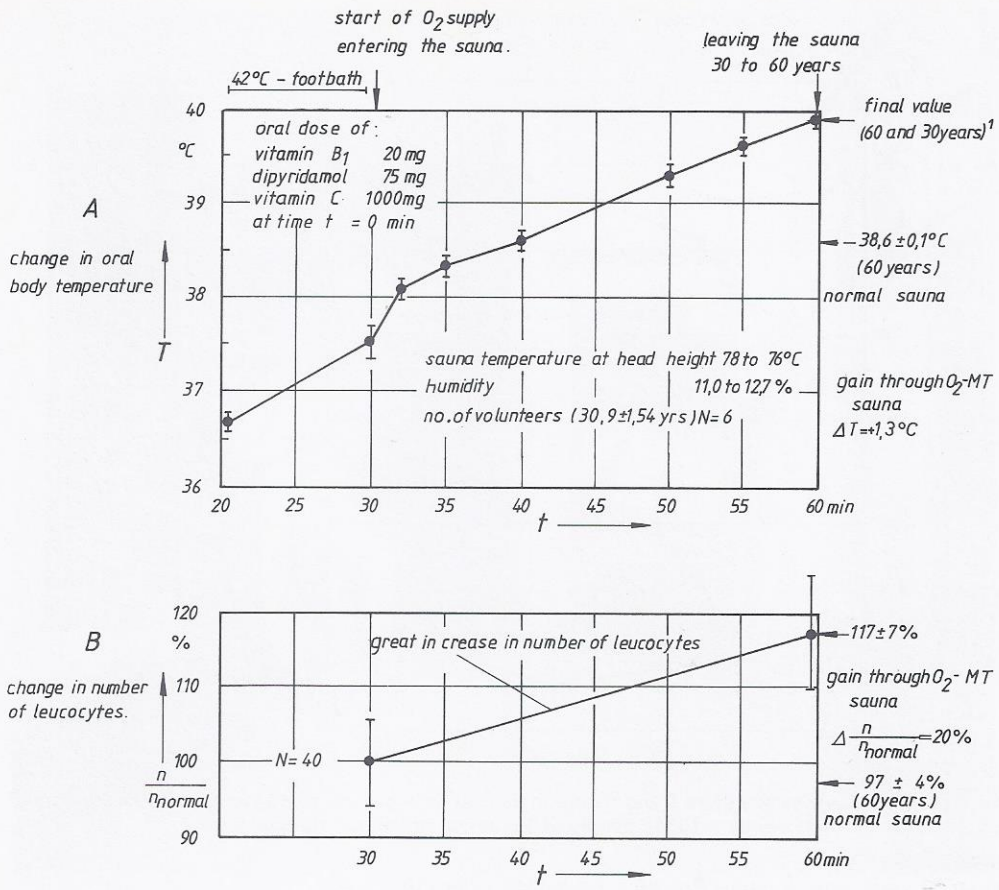


Fig. **222** Rise in oral body temperature T (A) and in the number of leucocytes n (B) as a function of the duration t of the visit to the O_2MT sauna according to [334]. Supply of 4 l O_2 per min via applicator. Result: Instead of after t = 10 min as in the normal sauna (increasingly felt circulation stress), the O_2MT sauna is not left until t = 30 min. As a result of this, even the age group of 60 years reaches an oral body temperature T = 40 °C. Simultaneously the number of leucocytes is 20% higher. A strong stimulation of the immunological defense system is caused by the O_2MT sauna, preferably when combined with daily administration of immunomodulators, such as thymus preparations (e.g. Neythymun) over the period of the O_2MT sauna cure

[1] Age group 30 years: arterial P_{O_2} during O_2 inhalation 127 ± 3 mmHg, pulse 115 ± 5 min^{-1}

The quick procedure, like the short procedure discussed in the following section, is *contraindicated* for patients with manifest or pronounced hypertonia (stage III/IV, WHO), with signs of cardiac decompensation, with stenocardia syndrome at rest and, to some extent, with febrile infections.

The procedure must be prematurely interrupted, if any dangerous signs during physical exertion occur (WHO recommendation). In connection with this we would refer the reader to the example in Fig. **224** which shows from the course of the pulse rate how an older patient in need of therapy could still be successfully treated with the 15 min O_2MT quick procedure by gradually altering the physical exertion before and during O_2 application (conditioning). The *increase in the physical performance capacity even during the O_2MT procedure*, which can also be seen from this figure, deserves great interest.

Many years ago, the former head of the 1st Medical Clinic of the Berlin Charité, our friend Theodor Brugsch, gave the author the following advice for the maintenance of good health in older age: "Be out of breath for 10 minutes each

day!" The deeper meaning of this recommendation was that once a day an increase in the O_2 metabolism of the cells and tissue and a periodic increase in the strain on heart and lungs were to be brought about. The 15 min O_2MT quick procedure and the daily minimal training demanded afterwards, as in Fig. **153**, fulfil Brugsch's recommendation. This procedure, already discussed in detail in Paragraph 1.1, and especially in 1.1.9.4, is the variant of the O_2MT which leads to the greatest increase in the O_2 metabolism in the endothelial cells of the terminal capillary bed, and as a result of physical exertion (increase in COP and RMV, highest O_2 flow taken up by lungs, highest $P_{O_2\text{-art}}$ during O_2 application, increased blood flow in capillaries). This means that this variant, with a duration of only 15 min, is sufficient for the "high-charging" of the blood microcirculation or of the O_2 uptake at rest.

The 15 min O_2MT quick procedure is a variant with weighty prophylactic indications, intended mainly for those who are still healthy or for those with functional disorders, and it should have a wide field of application in cure institutions (fitness centers). In healthy persons the increase in circulation occurring during physical exertion is accompanied, as the measurements in Fig. **225** show, even without additional O_2 application by an increase in the $P_{O_2\text{-art}}$. With O_2 application at a flow rate of 30 l/min $P_{O_2\text{-art}}$ levels of up to 350 mmHg (23.5 kPa) were measured, as documented in Fig. **3**.

After decades of regular sport in youth and middle age, the O_2MT should not be begun too late. Many of the pathological phenomena, which are caused primarily by O_2 deficiency or reduction in the resting $P_{O_2\text{-art}}$ and O_2 uptake, and which develop slowly in the course of many years, and which, after all, can determine the fate of the individual, are of *reversible character in their early phase*. The chance to set a favorable course by deciding to undergo prophylactic treatment before the symptoms of the disease become manifest therefore only exists for a limited period of time. Here, too, the individual can do a great deal in addition to therapy. The levels of the arterial and venous P_{O_2}, measured at rest, and the η-value derived from these, are high-ranking relative characteristic values for the O_2 situation, or the acute energetic situation. These values not only depend on age and therapy, but also on body mass. Figure **226** gives quantitative information on this. According to this figure, for example, the same reduced $P_{O_2\text{-art}}$ in a slim 20-year-old is to be expected as in a heavily overweight 45-year-old. Parallel to the use of the O_2MT,

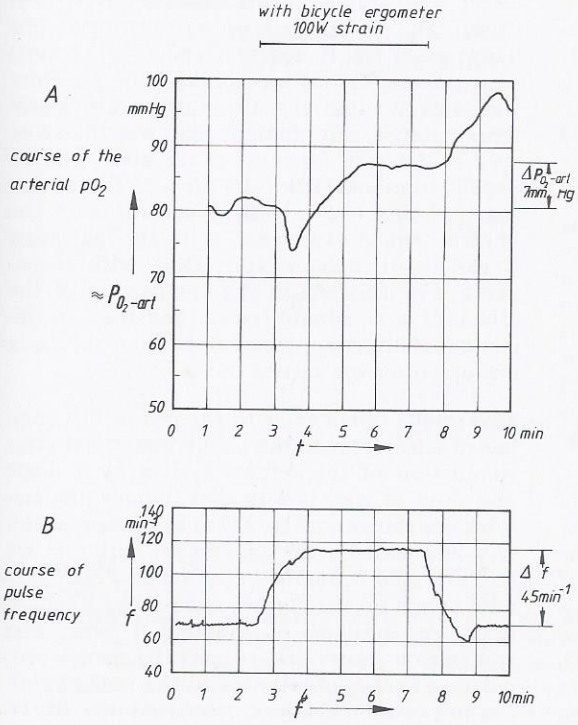


Fig. **225** Transcutaneous registration of the arterial P_{O_2} and the pulse frequency of a healthy 39-year-old man, breathing air, during physical strain of 100 watt for 5 min [255]

extra effort involved for the patients and doctor, we now always perform the 15 min O_2MT quick procedure in the GK 2-II variant with the administration of thymus dragees or NeyThymun drops.

Variant GK 2-III: In high fever (40 °C) with increases in the pulse rate from, e.g. 70 to 100 per min, there occurs an increase in COP from approximately 6 to 12.5 l/min. At normal temperature (37 °C) the same increase occurs with physical exertion of 60–70 watts. With this exertion or at 40 °C fever, an increase in the RMV from approximately 7 to 25 l/min is observed in normal, untrained persons. Approximately the same increases in COP and RMV are the physiological conditions for the discussed 15 min O_2MT quick procedure, GK 2-I, with physical exertion. The correspondence of the increase gave the author the idea of using advanced phases of fever for an O_2MT quick procedure with approximately 25 min supply of 25 l/min pure oxygen (via a mask applicator with storage balloon).

Figure **125** has already shown a summary of facts and measurements in the application of the O_2MT quick procedure with the utilization of high fever, in a typical example. Similar results were obtained in numerous further cases with high fever in various clinics advised on this point by the author.

The *programming of the 25 min O_2MT fever procedure, GK 2-III*, is extremely simple. As in all other variants of the O_2MT, the combination preparation Oxygenabund, or its components, is given orally roughly 30 min before start of O_2 inhalation, in order to improve the O_2 utilization in the body tissue. The O_2 inhalation is undertaken using a mask applicator with storage balloon for a duration of 25 min with an oxygen flow of approximately 25 l/min. The same mechanism which elevates the O_2 status occurs with this variant as in the 15 min O_2MT quick procedure, and the time required for rehabilitation from the state of debility is generally reduced to a few hours (cf. Fig. **125**). The process makes it possible to reduce considerably the danger of many illnesses in very old age. The practical application of this type of process is made much simpler by the fact that an increasing number of O_2MT treatment centers are beginning to provide mobile O_2 stations and that various projects are underway to make it possible to perform the O_2MT in the patient's home, in suitable variants.

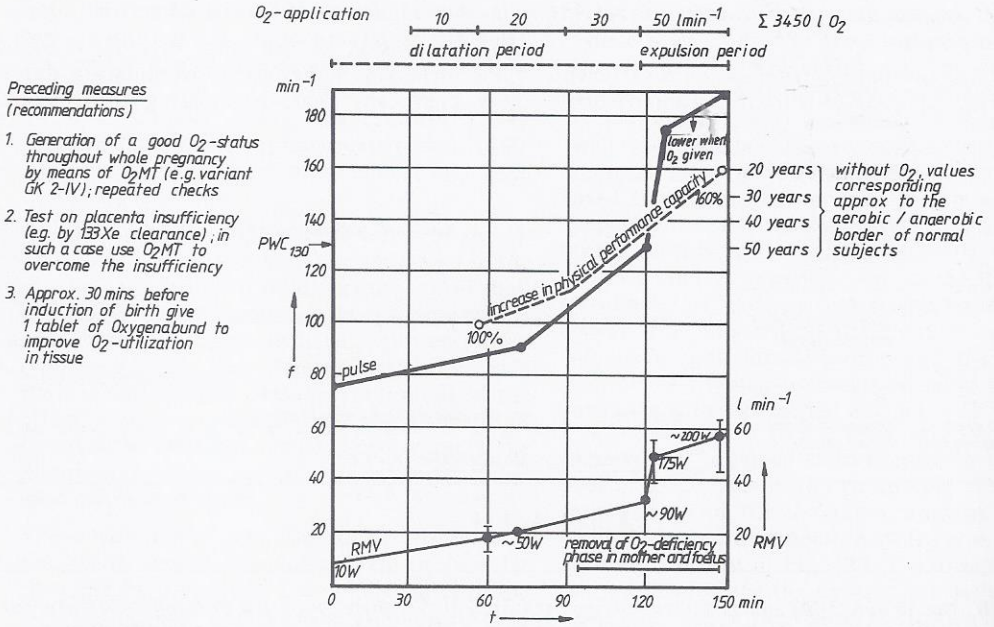


Fig. **229** Measures and guiding parameters demonstrating reduced risk and easing of births in women over 30 by means of the 120–60 min O_2MT obstetrics procedure GK-IV [348]. Mean values, valid for women of 70 kg b.w. and of average physical fitness, derived from RMV measurements by D. Petzold and H. Bellee on 12 women during parturition (Gynecological clinic, Director: Prof. Dr. M. Link, of the County Hospital Dresden-Friedrichstadt)

Variant GK 2-IV: The concept of the 120–60 min O_2MT obstetrics procedure [18, 348] is methodologically closely related to that of the 25 min O_2MT fever procedure. A naturally existing great increase in COP and RMV is again used to increase the O_2 status, and thus also the physical performance capacity, by means of the triggering of the switching mechanism of the blood microcirculation during and after the procedure.

It hardly needs to be pointed out that the *birth process*, from the beginning of the labor pains right up to almost the end, exhausts the woman's strength and energy reserves. This applies even more to women over 35 or with existing diseases, in whom the energetic status has already sunk noticeably compared to the status in youth. During the expulsion phase (RMV up to 60 l/min) critical energy, i.e. oxygen, deficient conditions can therefore often arise in the child, which is still supplied from the mother. It is known that this deficiency can cause damage of a considerable proportion of the child's brain cells. The measures summarized in Fig. **229** should be applied in order to prevent these deficiency phenomena which can have drastic effects on the child. In the mother there occurs a significant increase in the physical performance capacity in the expulsion phase (150–200 watts) due to the increased production of chemical energy (energy-rich phosphates, process of birth shortened). In addition to this there is a lasting improvement in the O_2 status of her organism after birth, caused by the triggering of the switching mechanism of the blood microcriculation (the resting value of η is roughly doubled). Pilot treatments were so favorable that they have been continued. During administration of 50 l O_2/min no critical increases in cord blood P_{O_2} were observed. The brightness of the mothers after birth was particularly striking. If the measures given in Fig. **229**, left, are also applied (combatting of placenta insufficiency by previous O_2MT treatment), there should be a better situation for women between 35 and 45 in this question in future.

4.2.3 9 h oxygen multistep therapy short procedure GK 3 and GK 3-I

The *program of the 9 h O_2MT short procedure, GK 3*, is presented in Table **26**. In this short procedure the O_2 application occurs via a mask applicator with storage balloon and of a flow of 6 l O_2/min. The increase in the COP and the correlating RMV is brought about in these short procedures by stimulating drugs, e.g. sympathicomimetics such as Mesocarb, Dopamin analogues, Alupent (cf. Table **14** and Fig. **140**). This variant is therefore mainly intended for the large number of patients who are not, or not sufficiently, able-bodied or who, for various reasons, cannot undertake or tolerate physical exertion.

The *main indications for the O_2MT short procedure* are, e.g.:

1. Bringing the patient out of general debility or unconsciousness
2. Speeding up of rehabilitation
3. Stabilization of the circulation in motor-paralyzed patients
4. Stabilization of the circulation in immobile patients
5. Stabilization of the circulation in physically disabled patients
6. Building-up of energetic reserves before foreseeable stress
7. Elimination of side-effects of "doping" drugs
8. Aid in resuscitation from coma lasting several days
9. Immediately after stroke, to reduce deficiency symptoms

Contraindications have already been discussed in Paragraph 2.3.3.

Variant GK 3-I: 5x20 min O_2MT short procedure with lasting effect for sufficiently mobile patients with adequate stress capacity but with little time. See Appendix for programming. The RMV is increased to 12 l/min by means of moderate physical exertion during five 20 min sessions taking place within say 5 days (roughly 40 watts, supported, if necessary, by administration of one 20 mg Alupent per session). The O_2 flow is adjusted to also 12 l/min, using a mask applicator with storage balloon.

In terms of effect ($P_{O_{2\text{-art}}}$, $P_{O_{2\text{-ven}}}$, η, O_2 uptake) and time required, this variant lies between the 15 min O_2MT quick procedure discussed in the last paragraph and the 36 h O_2MT (standard) procedure dealt with in the next. In patients who would normally be given the 36 h variant but cannot spare the 18 (or 9) days for it, and still have a moderate stress capacity, the increase in circulation necessary for the short procedure can also be brought about by slight physical stress. This is a fruitful field for further

research. Experiments with this method (if necessary, supplemented by the O_2 activation method or HOT*) to *resuscitate patients from unconsciousness of a certain pathogenesis, lasting several days*, would also be interesting (colloquium with H. Gerstenbrand, University of Innsbruck, Austria, on 11.11.82).

4.2.4 36 h (18 day) oxygen multistep therapy procedure, GK 4-I, GK 4-II, GK 4-III and GK 4-IV

Variant GK 4-I: The *program of the 36 h (18 day) O_2MT procedure, GK 4-I*, is given in Table **27**. It is the procedure [2, 3, 6, 20, 92, 159, 337, 338] with which the lasting restoration of the $P_{O_{2\text{-art}}}$, at rest, which had sunk greatly in older age, was surprisingly discovered in 1977 [3] and in 1982 the similarly lasting reduction in the resting $P_{O_{2\text{-ven}}}$ [338]. It is also the variant which has so far been most frequently used on patients (sort of standard treatment) and which has been the most thoroughly studied (see Paragraph 1.1.8.4 ff). The sensible total duration of the procedure was set at 36 h because the $P_{O_{2\text{-art}}}$ level (cf. Fig. **39**) and the $P_{O_{2\text{-ven}}}$ level did not improve with a greater number of hours. When well organized (2 min exercise every 20 min, mask applicator etc.), the time required for this variant can be reduced to 30 h of treatment within 15 days. It enables the patient to adapt better to the normal 3-week cure course. This rather time-consuming variant has the advantage that a particularly strong increase in the resting $P_{O_{2\text{-art}}}$ is observed with it (strong lung regeneration), and that it can also be used for patients with little stress capacity and who are disabled. Three types of timing of the procedure are preferred at present: *a 9-day cure with 9 sessions of 4 h* (out-patients and in-patients), the *18-day cure with 18 sessions of 2 h* (usually for outpatients) and the *5-night cure with 5 treatments of 7 h* during sleep (in-patients).

Indications for the 36 h O_2MT procedure are:

1. Regeneration of the lung-heart system, universal prophylaxis
2. Support for the drug treatment of heart and circulation
3. Oxygen deficiency diseases
4. Diseases and complaints of old age, senile diabetes
5. Angina pectoris, cardiac arrhythmias
6. Retinopathies, loss of visual field, light sensitivity
7. Sudden reduction of visual acuity, cataract
8. Not yet established hypertension (stages I and II WHO)
9. Arteriosclerosis, coronary sclerosis
10. Peripheral circulatory disorders
11. Disorders of the energy balance of the brain, defective memory, migraine, sleep disorders
12. Liver, especially when damaged by alcohol, cirrhosis of the liver
13. Disorders of the kidney function
14. Chronic bronchitis } as supplement to conventional therapies used in the individual case
15. Lung emphysema } as supplement to conventional therapies used in the individual case
16. Speeding-up of rehabilitation, wound healing
17. Alleviation of toxic stress and the side-effects of aggressive drugs
18. Increased physical and mental performance capacity, and quality of life
19. Combat of placenta insufficiency

The 3rd step of the program will be chosen very differently according to the stress capacity of the cure participant. Good circulatory condition is often sufficient in this long-term variant to reach the desired increase in the η-value. If the patient is able to tolerate it, coffee should be drunk in order to increase the $P_{O_{2\text{-art}}}$ and the COP slightly. The *supplementation of the program by exercise training in the intervals between the treatment sessions is obligatory*, except for disabled patients; see 2.3.7 for the type of exercise training. For non-able-bodied patients, a low dose of Alupent is given before each session.

In special cases, e.g. in patients with a very low pretherapy level of the $P_{O_{2\text{-art}}}$, in whom it is important to achieve an additional intensification of the regeneration, it is recommended that the O_2MT procedure be performed in the variation with 6 sessions of 2 h per week over 21 days, and that it be supplemented by a dose of 14 mg *Buphenin hydrochloride retard*, i.e. one capsule Penitardon three times daily (e.g. at 7.00, 15.00 and 23.00 hours). This recommendation is based on an experiment with similar medication and similar timing on 10 patients with a mean $P_{O_{2\text{-art}}}$ of hardly 50 mmHg (angio-organopathies of the most varied location, in stages III and IV according to Fontaine), whose $P_{O_{2\text{-art}}}$ rose to 80 mmHg with this medication [349].

In cases of increased resistance to therapy in chain smokers with up to 15 % CO poisoning of the hemoglobin, it can be necessary to perform an Hb detoxification [18] before the procedure and even to raise the total number of treatment

hours to up to 60. Conversely, it is often possible to reduce the duration of treatment, e.g. to 18–24 h, in patients in whom the O_2MT procedure must be repeated due to stress.

The tremendous speed with which the 36 h O_2MT procedure has been absorbed into healing practice allows us to conclude that the O_2MT should soon become a *universal methodological element of the cure system*. Its prophylactic effect is unusually broad because this procedure, as stated in the introduction, attacks the primary causes of many complaints and diseases.

With the developed zeolite devices whose performance is adapted to the high demand of the main variants of the O_2MT, equipment has arisen which, powered from the mains, provides inhalation air with increased O_2 content by means of oxygen enrichment of the atmospheric air (see Paragraph 3.2.4). Thus the time is approaching when air mixtures with a high O_2 content will be easily available even in the home. In the near future, therefore, the technical requirements will be met that will allow patients in need of O_2 to be able to apply variants of the O_2MT, of a gentle nature, in their private sphere under medical advice. One of the most important of these variants is the *O_2MT sleep*.

The idea of using the apparently unproductive sleeping time of a human prophylactically and therapeutically in an intensive way is fascinating. It is really true, for example, that a person in old age can in this way increase his O_2 status far above the best levels of his youth for 6–8 h of the 24 h cycle. It is also an enticing feature of this variant that it consumes no active time. A press of a button on the device switch before falling asleep is all that is required, and then the time spent asleep is used multivalently in the interests of health. An in-built switching-off system in the device ensures that, after a selectable period of time, e.g. 7 h, the current is automatically switched off, and the remaining sleeping time is spent normally.

In order to smooth the path towards the broad utilization of this variant, a technical task had to be performed: the *nonintrusive application of the O_2-air mixture*. The only technical solution that was admissible was one that would not be felt to be disruptive when falling asleep and that would not disturb sleeping habits. We believe that the mask applicator of soft synthetic material (with storage balloon), shown in Fig. **166**, is a very good solution to this problem. A soft pillow is all that is needed to prevent the synthetic tube of the applicator from being a nuisance when the patient lies on his side.

The 5-night sleeping cure is mainly suitable for persons under great stress (State officials, industrial managers etc.), who spend too little time on maintaining their health, yet are under extreme stress over a period of years. When their cure is suitably organized they can work at full capacity during the day and, due to the nightly 7 h treatment time, this variant consumes no productive time.

Variant GK 4-II: After the addition of measures to increase lastingly the COP by means of daily minimal heart training during the 18-day cure, there results a variant with the term *36 h (18 day) O_2MT procedure and minimal training* [37]. The concept of this variant is based on the result, presented in Figs **66–68**, that the critical deterioration in the O_2 status with advancing age is due almost entirely to the drop in COP. It can be seen from sports medicine and, especially from the papers by Hollmann and his team in Cologne (FRG), to what extent and in what way the drop in COP can be alleviated by stamina training and sport in old age [269, 270]. A *cardiopulmonal minimal training* could be derived from these papers, which could be included in the 36 h (18 day) cure without any increase in the amount of treatment time required.

The program of the 36 h (18 day) O_2MT procedure and minimal training (GK 4-II) can be seen from Table **28**. The decision whether to include the dose of Alupent (optional) rests with the doctor in charge. The minimal training of ten or 2x5 minutes duration, inserted at the end of the 2 h session, as in Fig. **230**, takes place without O_2 application and aims at an increase in the pulse rate of f = 180 minus age (Hollmann's rule), characteristic for the aerobic/anaerobic threshold [270]. The inclusion of the minimal training in the framework of the 2 h session has the advantages of being easy to control and of eliminating additional time required. If these two aspects are unimportant, the minimal training, because it occurs without O_2 application, can also be undertaken somewhere else and at any convenient time, in accordance with the guidelines in Fig. **153**. Such a process has the advantage that the patient becomes accustomed to such training in his own environment and is then more likely to continue the same minimal training daily for the "energetic lifestyle" demanded.

The main *indications of the GK 4-II variant* are:

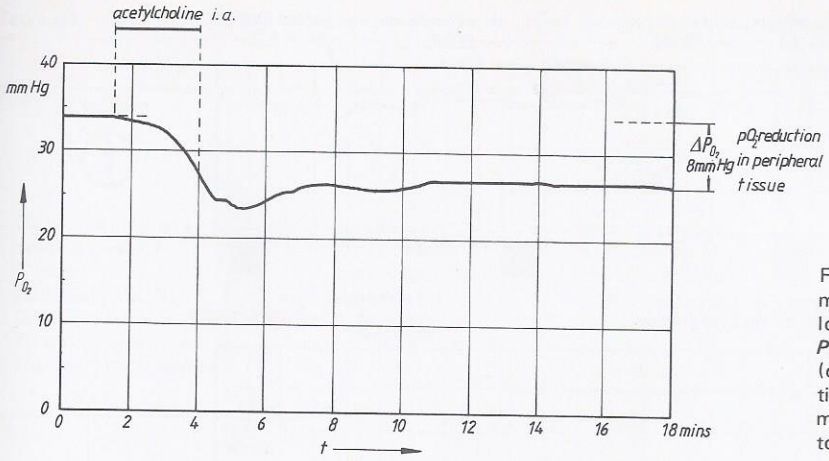


Fig. **232** Small-area P_{O_2} measurement showing the long-lasting reduction of P_{O_2} in a peripheral tissue (dog tail) after centralization of the circulation by means of the vasoconstrictor acetylcholine [309]

1. Fast aid in emergencies of all kinds
2. Amelioration of consequences of strokes
3. Combat of shock when still in its reversible early phase
4. Severe concussions of the brain
5. Aid in severe toxic stress
7. Aid in high fever, especially in older patients (also at home).

The supporting of the circulation using O_2 is a standard medical process, especially in anesthesiology. The O_2MT support of the circulation can therefore be seen only as a somewhat increased form of a standard procedure, albeit with greatly extended range of indications.

Figure **233** shows an example of the effect of the *O_2MT circulatory support in circulatory stress*, by means of 40 °C/250 min whole body hyperthermia. The hyperthermia in a hot water-bath, lasting over 4 h, signified a very great strain on the circulation which even in individuals having an intact cardiovascular system, normally leads to precollapse stages. This is shown in a critical drop in the blood pressure amplitude towards the end of the hyperthermia phase (Fig. **233** A), as we observed in numerous volunteers with former CMT technology [2]. This drop in the blood pressure amplitude does not occur when the O_2MT circulatory support is applied during the phase of hyperthermia (Fig. **233** B). This finding is to be expected from the viewpoint of the physiological bases, because, as already shown in Fig. **124**, a significant reduction in the O_2 saturation of the blood occurs with an increase in temperature from 37 to 40 °C or higher, especially in older persons. It is therefore very obvious that the O_2MT circulatory support should be applied during attacks of fever (even at home), when weakened or old patients are affected. The fast fulfilment of this demand will frequently prove to be life-saving. As the febrile episodes usually last only a few hours, O_2 provision from small, portable pressure cylinders is generally sufficient here.

The *optimization of the O_2 supply to the brain before and during major operations* is a very important indication. In order to achieve resynthesis of energy-rich phosphates, adequate for the situation, it does not suffice to begin artificial respiration with additional O_2 10 minutes before the operation, as is generally the case today. Our experiments with laboratory animals [4] have shown that, in order to achieve maximum recycling of energy-rich phosphates in the brain, O_2MT circulatory support should begin 120 min before the start of the operation. Measurements in experiments with laboratory animals of the drop in the concentration of energy-rich phosphates after the end of the O_2MT procedure (cf. Fig. **133**) have shown that, even after 4 h, the level of ATP is still 10% above the normal level. The stabilizing effect on the metabolic O_2 requirements of the brain, the maintenance of the functional stability of the blood-cerebrospinal barrier and the achievement of a sufficient clearance function for acidic metabolites by an O_2MT-stabilized circulation, should therefore last for some hours after the end of the procedure.

It is to be concluded from impressive case reports [351] that the *consequences of acute cerebrovascular insufficiencies can be ameliorated* if the O_2 situation is improved, using this variant, as soon as possible after the onset of the circulatory disorder, especially before manifestation of the consecutive perifocal brain

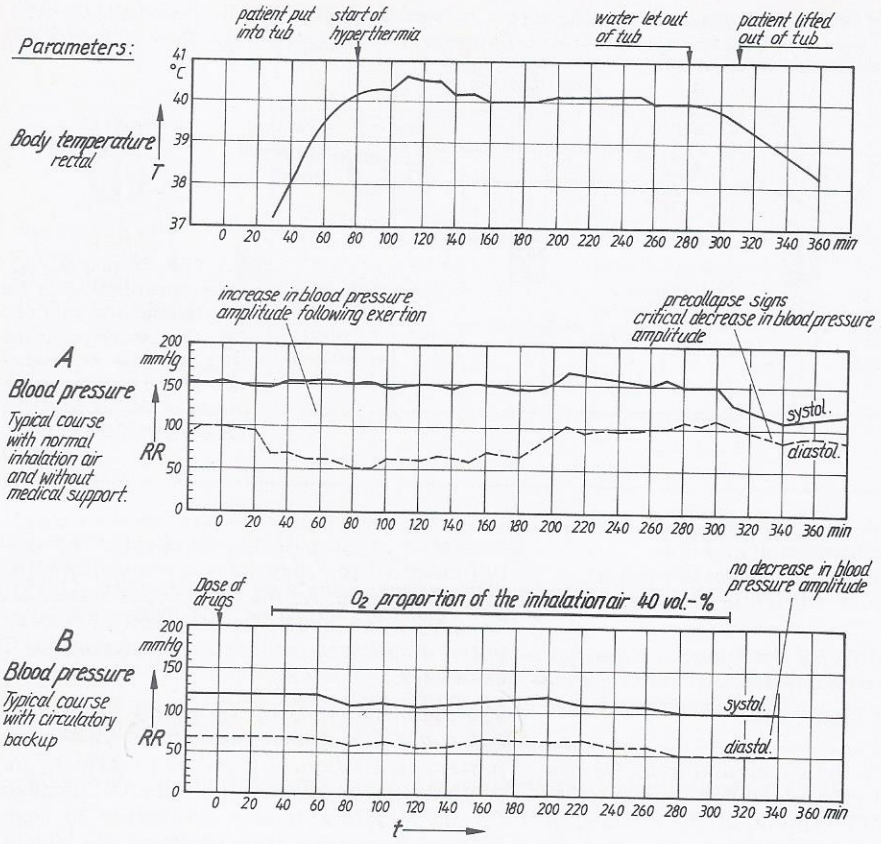


Fig. **233** The effect of circulatory backup by means of O_2MT after circulatory disorders due to a 250 min 40 °C whole body hyperthermia

edema. Such findings encourage us to hope that the consequences of transitory cerebral ischemia can be weakened in this way. In the first few weeks after severe cerebral circulatory disorders and cerebral ischemia it should also be attempted to strengthen the tendency to restitutio ad integrum, e.g. by O_2MT sleep and supplementation by HOT*.

4.2.6 Oxygen multistep long-term aid GK 6

The *program of the O_2MT long-term aid* [2, 4, 352, 353] can be seen in Table **31**. The characteristic of this variant is that an O_2 flow of approximately 2.5 l/min is given to the patient for very long periods and, most importantly, without intermissions over the 24 h daily cycle, using the comfortable nozzle applicator or mask applicator of soft synthetic material (with storage balloon). The specific feature is that the O_2 status is further raised by taking 2 Oxygenabund tablets daily (1st step) and moderate regular exertion.

Examples of *indications for the O_2MT long-term aid procedure are*:

1. Partial respiratory insufficiency: chronic obstructive and chronic inflammatory lung diseases, degenerative loss of function, infectious lung diseases, postoperative conditions such as lobectomy and pulmectomy, formation of thickenings, cicatricial scars, permanent shortness of breath [354, 355]
2. O_2 deficiency diseases: ischemic diseases of organs such as heart and brain, or of functional units of organs such as gastrointestinal tract or the sense organs
3. Long-lasting unconsciousness (cf. also Paragraph 4.2.3, aid for resuscitation)
4. Intensive nursing cases.

5.1.2 Symptoms and causes of disease. Combat of falling ill

Most prophylactic and therapeutic measures today still aim to influence symptoms recognized in complex systems of the living organism, and their control. Future medicine will not so much be concerned with only the *symptoms of diseases* in this way, as with applying itself against the *causes of the diseases*, supported by measurement, calculations and biomedical technology. The common causes of the diseases and potentially fatal crises lie, much more often than generally thought today, in deficiency conditions (energy deficiency, usually caused by O_2 deficiency) with alterations of the cells or cell organelles of the organism and its organs. *The temporary or lasting positive influence of the metabolism of the cells, in conjunction with biotechnical means and controls, therefore represents a weapon of fascinating universality against large groups of diseases and crises.*

A particular important example of the utilization of this principle for health care is the combat of the many O_2 deficiency diseases and crises which not only occur in older age, but also as a consequence of environmental conditions that are constantly deteriorating (lack of exercise, stress, air pollution) and becoming very much more significant. The different variants of the O_2MT discussed form a specific tool against these. Despite its very great efficacy, however, this tool is as yet only slightly acknowledged and applied.

Moderate arterial hypoxemia, such as is observed in bed-ridden or paralysed patients with sound lungs, for example (extreme lack of movement), also has great pathogenetic significance: to begin with, the relative slight hypoxemia is disguised by circulatory and ventilatory compensation mechanisms. This results in local vasodilatation in the most important organs, increased cardiac output (COP) and intensified ventilation, in order to secure a sufficient delivery of O_2. The coronary vasodilatation is of critical significance here. If the increase in COP is insufficient, a further deterioration in the hypoxidosis occurs, which most affects the myocardium and the brain. The vicious circle is clear. In such cases, therefore, even slight reductions in the O_2 offer to the body tissue (reduction in the product $\eta \cdot$ COP), which neither lead to cyanosis nor, as a rule, are defined as arterial hypoxemia, are often dangerous [92]. This is particularly the case when there are only slight cardiac performance reserves. The consequences are, at first, hypertonia, tachycardia and, later, hypotonia. The O_2MT is strongly indicated if these symptoms appear.

The real field of application of O_2MT lies long before the combat of diseases and crises: it is the *prevention of falling ill, by maintaining a high level of energy provision for the organism and its defense system throughout the whole of human life.*

5.1.3 The four temporal effects of the oxygen multistep therapy

1. Effect during the procedure. Particularly strong effects during the procedure are to be expected where the O_2-enriched respiratory gas or the increased $P_{O_{2\text{-art}}}$ (cf. Fig. 7) work out directly (not weakened by the typical course in the upper part of the HbO_2 dissociation curve). This applies to the alveolar system of the lung, for the artery walls, for the lens of the eye, i.e. to *systems where the pressure gradient of the O_2 diffusion is mainly determined by the arterial P_{O_2}*. The other direct effect during the procedure is the *increase in the P_{O_2}, even at and near the venous end of the capillaries* (cf. Fig. 3).

The previously mentioned improvements in the P_{O_2} levels have long been utilized as *monentary effects* within the framework of the standard measures of O_2 application in medicine (intensive care units, emergency service, combat of acute O_2 deficiency crises, prophylaxis of shock, long-term help for patients with advanced lung insufficiency etc.). An important momentary consequence of the rise in the O_2 status is a significant *rise in physical performance capacity*, which measurements show to increase during the procedure. The increase enables the patient to undergo physical exertions during the procedure, which he would often be unable to do without O_2 support (e.g. O_2MT quick procedure, O_2MT obstetrics procedure). This rise in physical performance capacity also makes it possible to *achieve physical performances in the short intervals between the individual sessions, which the organism normally cannot or can no longer achieve* (O_2MT short procedure).

These momentary effects must be strictly distinguished from the *integral effects*, which are

the most important part of the O_2MT as they alone bring about the effects which endure long after the end of the procedure. The high-charging of the blood microcirculation by the reversal of the endothelial cell swelling, which has occurred in hypoxia, is of prime importance here. The momentary effects during the procedure end to some extent in a *functional regeneration of the systems or organs* (lungs, heart, vascular system etc.).

2. Fading effect after end of procedure. The fading effect was discovered in 1971 when energy-rich phosphates (ATP, CP) were measured in the brains of rats [4]. It was found that the ATP and CP concentrations rose after 90 min O_2MT treatment from 100 to approximately 165%, and only faded to approximately 112% 180 min after the end of treatment (cf. Fig. **133**). This method to induce the resynthesis of energy-rich phosphates for some hours has been clinically used in major brain operations in Dresden. This improved provision of energy immediately before foreseeable severe stress (operations, births, special performances by singers, politicians etc.) could in future be an aid which is also strongly felt subjectively.

3. Immediate effect of the lasting, great increase in the O_2 status. We define as *immediate effects* those lasting increase in the O_2 uptake of the body tissue and in the CO_2 production, and their consequences, which are measured or observed after a successfully completed O_2MT procedure. It almost goes without saying that these immediate effects are stronger, the worse the initial O_2 status (the higher the age and the more pronounced the deterioration in status due to stressful influences). Typical examples of frequently reproduced immediate effects are: increased circulatory stability, elimination of orthostatic symptoms in hypotonia, drop in the – mainly systolic – blood pressure in essential arterial hypertonia (stages I and II, WHO), drop in blood sugar levels in senile diabetes, combat of migraine, Morbus Ménière, Ménière's syndrome and hemicephalgias of unknown origin, night-time cerebral ischemias with disturbances of the sleeping-waking rhythm[1], reduction in the visual and accoustic reaction time, subjectively felt improvement of many symptoms of chronic IHD (= ischemic heart disease), reduction in the activities of dystrophic enzymes in damage of the liver parenchyma, elimination of dysopsies, increase in body defense system, general increase in vitality, and the lasting, measurable increase in the physical performance capacity (double blind study [61]).

4. Long-term effects of the lasting, great increase in the O_2 status. *Long-term effects* are the result of maintaining an O_2 supply to all tissues, organs and systems of the organism consistently above the expected level over a period of years and decades, using O_2MT. The time since the discovery of the lasting effect of the O_2MT (1977) is too short to allow definite statements on this important question. A growing number of individual observations point to a postponement of physiosclerosis and of the ageing of the skin. The next paragraph discusses the reasons that justify our hope that human life can be prolonged and made worth living for longer by the maintenance of a high O_2 status with as few interruptions as possible (frequent $P_{O_2\text{-art}}$ control measurements, O_2MT as soon as a reduction is ascertained).

[1] The change from waking to sleeping (and vice versa) is an energy-requiring (O_2-requiring) process

5.1.4 Stimulation of defense against diseases and reduction of their danger in old age as ways to approach the maximum biological age of the human organism

The aim of the O_2MT is to influence positively the life of the individual by the application of variants adapted to his needs. Figure **236** gives examples of the human life-span with various pathogenetic disturbing factors. Positive influence means the *reduction of the frequency and danger of illnesses, increased life expectancy and an increase in vitality and hence also in the physiological age*. In this goal we see no contradiction to efforts to limit the population of our planet. Great progress for society can always flourish when the experience and wisdom of the old combine with vitality and creative power.

According to Fig. **236** the genetic program of the human organism should not lead to death before the age of 120 years [369]. In reality, the pathogenic disturbing factors and their simultaneous occurrence in the late phase of life in the framework of polypathias cause a much earlier end to life. To supplement our presentation we can include a result gained by

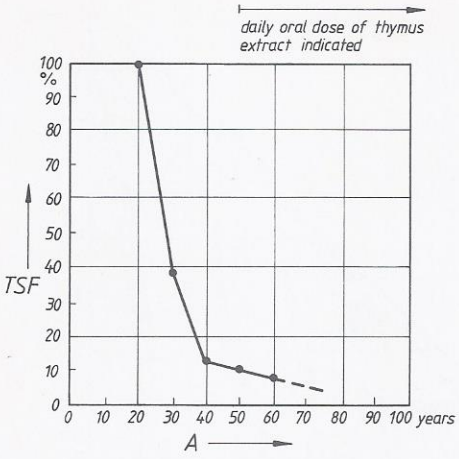


Fig. **239** Thymus serum factor TSF dependent on age A (according to Astaldi 1975)

For the first time in the history of medicine there is the prospect, founded on measurements with statistical significance, of securing *even for very old people a good O_2 status* lasting for many months and even, with regular repetition of the procedure at reasonable intervals, *permanently*. At the same time this effectively combats the hitherto fatal increase in susceptibility to, and in the danger of, diseases in old age. The processes with this effect are the variant GK 2-II, the 15 min O_2MI, and the variant GK 4-IV, the 36 h (18 day) O_2MI, discussed in detail in Paragraphs 4.2.2 and 4.2.4, respectively.

Looking back at the discussed combinations of measures to reduce the susceptibility to, and the danger of, disease in old age, a common principle becomes clear, i.e. the simultaneous energetic and hormonal strengthening of the natural healing powers of the human organism. The body is strengthened to a degree hardly thought possible before, thus corresponding to Hufeland's (1762–1836) old recommendation to strengthen the organism as a means of combatting health crises.

Figure **240** summarizes the *measures to improve the prospects for the attainment of an old age with good quality of life*. The fitness measures recommended change significantly with advancing age. Up to the age of approximately 40–45 years, regular sport or 10–15 min daily cardiopulmonal minimal training is usually enough to ensure a good O_2 status. From the age of 40–55 years the O_2MT variants GK 2-II and then GK 4-IV are increasingly indicated, the more the mobility and inclination to undertake regular exercise training decline. The following aspects must be particularly observed in the second half of life:

- Permanent securing of a good O_2 status, increase in circulatory reserves (reduced danger of illnesses) and maintenance of a good defense status (reduced susceptibility to illness) by means of O_2MI. Repetition of this procedure as soon as regularly undertaken P_{O_2} measurements show this to be necessary.
- In very old age, from approximately 90 years, regular additional implementation of the *O_2MT long-term aid*, variant GK 6, with an O_2 flow of 2.5 l/min during night-time sleep (O_2 provision from an O_2 Selector whenever possible), one Oxygenabund and one thymus Uvocal dragee at bedtime.
- 10–30 min exercise daily, so far as this is possible (division into 3 daily units if necessary). Exercise training in this late phase of life extends life expectancy.
- Due to stressful influences, e.g. infections, lack of movement, or diseases, the O_2 status drops to the greatly reduced level expected for this age. This means a transition to a life-endangering O_2-deficient condition. It is then of vital importance that no time is wasted in raising the O_2 status to a high level again using O_2MT variants adapted to the patient's condition (cf. also Fig. **237**).

For further measures favoring the attainment of a very old age, see [373]: energetic lifestyle, getriatric therapy, nutrition, gerohygiene.

To what extent it is possible to increase further the average life expectancy in populations with highly developed health sercices, above that of Fig. **241**, using the methods described here and with other methods with the same goal, remains to be seen.

5.1.5 Duration of the effect of therapy

The introduction of the special term "*oxygen multistep therapy*" is justified by the fact that a regeneration procedure of relatively short duration was unexpectedly discovered, which can significantly improve the O_2 uptake of the body and hence the energetic status for weeks,

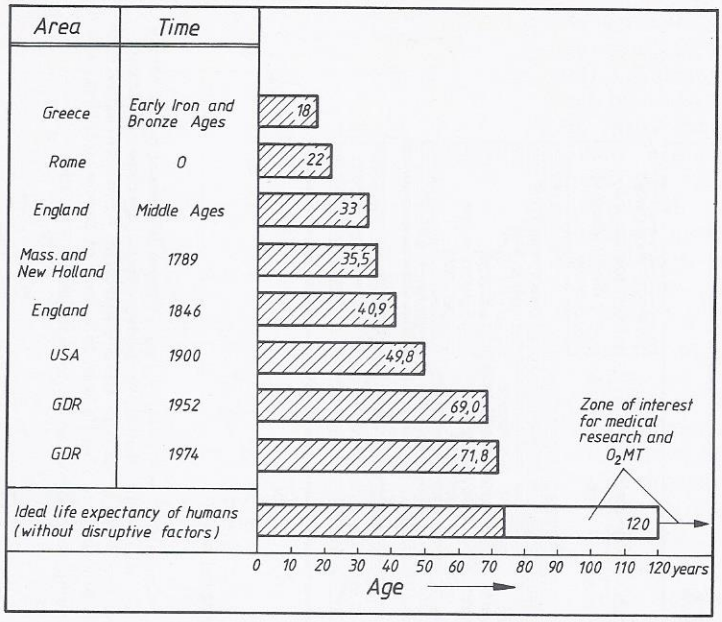


Fig. **241** Mean life expectancy of the population from antiquity to the modern age, modified according to [371]

months and even years after its completion. The term "multistep" was chosen to distinguish this therapy from the usual application of O_2 in medicine, because the *combination of several synergetic steps is the characteristic of all variants of the O_2MT basic procedure*.

Patients who have undergone the O_2MT rightly ask *how long the effect of therapy lasts and when the therapy should be repeated*. Patients often spontaneously registered themselves for a repetition because they subjectively felt the fading of the therapeutic effect. *A repetition of the procedure is always necessary when stressful influences have caused the level of O_2 uptake of the body to sink again considerably (recognizable from measurements of the $P_{O_2\text{-art}}$ and $P_{O_2\text{-ven}}$, at rest, for example).* The timing to a meaningful repetition of therapy therefore depends largely on the lifestyle and chance stressful events in the life of the individual.

It has now been proved beyond doubt that, with an energetic lifestyle (cf. Fig. **153**) without stress, the effect of therapy (increased product of $\eta \cdot COP$) can last for years. The measurement of the $P_{O_2\text{-art}}$, at rest, is generally enough to assess the maintenance or critical reduction of the O_2MT effect (cf. Figs **7** and **41**) because, as has already been pointed out, the change in the resting $P_{O_2\text{-ven}}$ is reflected in the dynamics of the $P_{O_2\text{-art}}$ (same mechanism in the capillaries of the lung and of the other tissue). Caspers [94] proved that the *O_2MT effect lasted for 18 months*, by measurements of the resting $P_{O_2\text{-art}}$ of 108 patients at his clinic. A relatively short duration of the effect of therapy can be observed in patients subjected to critical long-term stress. This applies particularly to patients who are paralysed or for any other reason not able-bodied, or disabled. In order to reduce the probability of additional diseases, O_2MT should be regularly repeated in these patients at intervals of 1–2 months, preferably on the basis of P_{O_2} measurements. The careful observance of this recommendation can prolong the lives of such patients. The regular repetition of therapy is of course made much simpler if the patient, advised by his doctor, uses one of the less strenous variants in his own home (e.g. GK 4-I, 5-night cure). For the large proportion of patients without long-term stress it is advisable to consider a repetition of therapy and to have the supervising doctor undertake P_{O_2} checks whenever there are stressful influences (see Paragraphs 1.1.8.3 and 1.1.9.3 or whenever an increase in complaints suggest a deterioration in the O_2 status.

The chances of successful therapy are greatly reduced in cases where the pathogenic factors have already been irreversibly fixed (e.g. definite vessel wall degeneration of arteries and arterioles, far advanced senile emphysema and other advanced lung diseases with loss of lung parenchyma). In such cases the bioenergetic control of the capillary wall switching mecha-

nism of the microcirculation no longer functions and an increase in O_2 uptake then depends only on the improvement in the steady state. In such situations (fixed disease) the patient must turn to permanent or long-term procedures (GK 6, O_2MT long-term aid).

5.1.6 Pathogenic consequences of oxygen deficiency and individual narrowings

Under the collective term "O_2-deficient conditions and O_2 deficiency diseases", in [2, 159] a survey of the conditions and diseases, whose primary cause must be seen in a long-lasting or chronic O_2 deficiency (energy deficit), was given. Which disorder out of the large spectrum is expressed first in each case depends on the individual situation of the organism and on the lifestyle and other peripheral conditions of the *pathophysiological bottleneck*. Thus, for example, random structural peculiarities in the vasculature in the organism can decide whether O_2 deficiency first leads to weakened sense organs, attacks of angina pectoris or cardiosclerosis resulting in cardiac infarction, or cerebral sclerosis with consecutive vascular thrombosis or cerebral hemorrhage, or whether circulatory disorders of the extremities first set in, resulting in gangrene, or whether the status of the host's defense system is so reduced that unrestricted growth of a malignancy begins [376]. It is not unusual for the localization of the deficiency in the organism to make itself felt early by subjective complaints. The observation of such *warning signals* should be seen as cause to begin prophylactic or therapeutic measures immediately. If the cardiopulmonal performance has dropped greatly, the number of sites of deficiency in the organism increases, and the phase of polypathias and multimorbidity (cf. Fig. **236**) begins toward the end of life. Conversely it follows from the great variety of pathological consequences of O_2 deficiency that a therapy such as O_2MT, that lastingly eliminates or alleviates O_2 deficiency, must possess (to an almost disconverting degree) the characteristic of *great universality*.

5.1.7 Indicated and contraindicated time points for the implementation of the oxygen multistep procedures

The inhalation of gas mixtures with increased O_2 content is normally applied in medicine in phases with poor circulatory condition, with the aim of temporarily supporting the circulation. Examples of this are the utilization of O_2 in emergency situations, in narcosis, in intensive care units and in severe chronic lung insufficiency. In such phases the circulation is particularly affected. The third step of the O_2MT concept is therefore absent or, more correctly, it is even of a negative character. This is the reason why the procedure with its long-lasting increases in the O_2 uptake and CO_2 production of the organism at rest, unexpectedly discovered in Dresden in 1977/1982, was not found much earlier, e.g. in intensive care units.

For the *O_2MT procedure to be successful* (crossing of the switching threshold, lasting increase in the post-procedural value of the product $\eta \cdot$ COP, for example) it must, by contrast to the above-mentioned O_2 application, be performed in *phases with as good a circulatory condition as possible* (selection of timing in daily cycle, increase in cardiac performance by means of stimulation or support, e.g. g-strophanthin, if necessary).

The treatment is contraindicated at times when spastic processes are occurring in the organism (e.g. attacks with severely increased blood pressure in hypertensives, migraine attacks or perhaps even angina pectoris attacks). Individual observations suggest that the treatment can cause an intensification of the spasms. The administration of spasmolytics may be considered according to the case.

The treatment of epilepsy using O_2MT is contraindicated because the effect of sedatives is more or less eliminated.

The measurement of the $P_{O_2\text{-art}}$ at rest and of the η-value should begin from the age of about 50 years, e.g. at intervals of 6 months at first, as a check-up. The O_2MT procedure should be applied as a preventive measure as soon as the results of P_{O_2} measurements show levels < 80 mmHg (< 10.6 kPa). This finally results in a *helathy lifestyle with controlled and optimized η or $P_{O_2\text{-art}}$* [20, 311].

O_2 MT institution (address): Dr. med. Hans Müller-Winter
CH-7320 Sargans

Patient (code): A.A. Age: 54 Sex: male Date: 5.7.1984

Clinical condition before therapy (if relevant, indicate Karnofsky index, BP, etc.)

After cardiac infarction: attacks of angina pectoris even during light physical exertion, also often when resting. ECG: biphasic T-waves V4-V6. Patient can only walk about 100 m without complaints; has been unable to work for several months.
Karnofsky index (KI): 65%

Diagnosis: State after cardiac infarction

Previous therapy:

O_2 status before therapy:	$P_{O_2\text{-art}}$	$P_{O_2\text{-ven}}$	η	$\dot{Q}_{O_2}$
Time of measurement: 9.00 a.m.	70 mmHg	35 mmHg	26%	1 · min $^{-1}$

O_2 MT variant: GK 4-I

O_2 status after therapy:	$P_{O_2\text{-art}}$	$P_{O_2\text{-ven}}$	η	$\dot{Q}_{O_2}$
Time of measurement: 9.00 a.m.	80 mmHg	30 mmHg	37%	1 · min $^{-1}$

Clinical condition after therapy (if relevant, indicate Karnofsky index, BP, etc.)
(Result of therapy)

Attacks of angina pectoris have disappeared.
ECG: nothing abnormal discovered.
Patient takes part in mountain rambles and is practically free of complaints.
Working again full-time in his career KI: 95%.

Fig. **242** Example of rehabilitation after cardiac infarction. Result of treatment

Table **35** Table of Karnofsky Index

Karnofsky Index	Criteria	Strain capacity
100%	no complaints	able-bodied
90%	slight symptoms of the basic disease normal performance	
80%	fully-developed symptoms of the basic disease normal physical performance only with effort	
70%	self-care, but no physical strain possible	performance limited
60%	partial help needed in self-care	
50%	help usually needed, partly bed-bound	
40%	predominantly bed-bound, hospitalization not necessary	self-care no longer possible
30%	completely bed-bound; no immediate threat to life	
20%	severely ill, hospitalization necessary	
10%	moribund	

5.2 Increase in physical performance capacity and combat of oxygen deficiency conditions

5.2.1 Increase in physical strength. Transition to a more energetic lifestyle

An increase in the physical performance capacity not only occurs after completion of O_2MT but rather, with almost all variants with advancing development of the switching process of the blood microcirculation, there is a continuous *increase even during the treatment*. This immediate response is of very great significance in the *120–60 min O_2MT obstetrics procedure*, GK 2-IV, because our measurements have shown that a performance of 150–200 watts must be attained by the mother during the expulsive stage. The increase is usually approximately 30% (duration of labor shortened, avoidance of non-vaginal deliveries). The increase in physical strength during the O_2 inhalation can be utilized to treat even patients who cannot cope with much exertion with the time-saving but strengthening 15 min O_2MT quick procedure, GK 2-I, under medical supervision. Figures **125** and **224** give examples of this. Figure **89** shows an example in which a great increase in physical performance capacity in an infarct patient can be seen after just approximately 12 h of the 36 h O_2MT procedure, variant GK 4-I.

For the lasting increase in physical performance capacity after O_2MT the reader should refer to the double-blind study [61] and our spirometric findings [466] which show that a *lasting increase of 15% (healthy persons) to 80% (weakened persons) in the CO_2 production at rest can be observed after O_2MT* (the CO_2 production is roughly proportional to the formation of energy-rich phosphates). This fascinating results accord well with the ergometric observation in Fig. **24**. It is a *basic demand of the O_2MT that this gain in physical energy be utilized for the more energetic lifestyle* (new formation of muscle). Even the smaller increase in strength in healthy individuals can help singers and actors before major performances, for example, or politicians and managers before particular events. The lasting increase in strength attainable could well determine victory or defeat in sporting competitions. The coach of a football team that undertook two treatments with the O_2MT GK 2-I variant in the Klinik für Naturheilverfahren in Bad Füssing, FRG, (Dr Caspers) a few days before each major match, twice informed the author of victories against far superior opponents and of his players' surprising concentration and freshness in the second half.

5.2.2 Oxygen multistep therapy and erectile dysfunction (impotence)

The author has received several reports of an *alleviation of impotence* after O_2MT. These observations suggest that it is useful to combine the O_2MT, which considerably increases the physical performance capacity, with the SKAT method [378] developed by Bähren and colleagues (University of Ulm, FRG). With this method an *alpha blocker* and *papaverine* are injected in both cavernous bodies. The alpha blockers serve to dilate the pelvic arteries in order to increase circulation there. Papaverine facilitates the unhindered influx of blood into the penis by relaxing the musculature in the walls in the cavernous bodies. The erectility lasts, according to findings by Wehnert (Urological Clinic, Medical Academy of Dresden, GDR), approximately 60–120 min. The practical process, cf. [378], is as follows: the injection solution is made up of 30 mg papaverin hydrochloride and 1 mg phentolamine methane sulfonate (Regitin, from Ciba-Geigy, Basle, Switzerland) in 2 ml sterile physiological saline

The corpus cavernosum is punctured right and left laterally from the dorsal middle of the root of the penis, vertically at a depth of 10 (to 5) mm using a disposable needle 0.45•13 mm (Sterican G•1/2″) under sterile conditions (disinfectant spray). The dosage varies between 0.05 and 3.0 ml of the given solution, depending on the extent of the erectile disorder. Prolonged erection over several hours can occur as a relevant side-effect (antidote). The age-limit of the Ulm autotherapy, which until now has ended at approximately 60 years, is increased by 20–25 years by combination with O_2MT (significant increase in physical performance capacity).

A new *vibrating injection syringe*, developed by Roggenbuck and the author for this purposes, can be of help in this problem. This syringe has the following features: an electrically driven motor vibrator sets the fine cannula of a disposable syringe into axial swinging motions, so

the cannula enters the required depth of the tissue (10 or 5 mm) virtually painlessly. First the front plate of the injection unit is placed on the selected tissue surface. Then the small motor drive pushes the vibrating needle through an opening in the front plate to a stop that determines the depth of the injection, and finally the same drive pushes the plunger of the 2 ml disposable syringe forward. The total time required for this is about 15 s. This new type of syringe with its low pain function should prove to be useful in several branches of medicine. A *special double syringe* with this operational method (GDR patent pending) adapted to the above task has also been developed. It has two axially vibrating needles, separated by 14 or 11 or 7.5 mm, which are fed via a T-tube from a 2 ml syringe. The needles, tube and syringe are all disposable. After the cylindrically shaped front part has been placed from above on the dorsal corpus cavernosum tissue and a small switch has been operated, the double injection process with its discussed functions runs fully automatically.

In the following detailed discussion of fields of operation of the O_2MT, the reader should recall the reservations expressed in the preface. We only have experience with larger numbers of patients with a few, albeit important types of application. With other types of application the positive results of a small number of individual experiments only justify hopes. With a further group of types of application we do not as yet have any practical experience. Nevertheless, we should not fail, in the framework of this book, to recommend that they be tried, because positive effects are to be expected in accordance with the underlying physiological processes. The relevant paragraphs therefore signify nothing more than an encouragement of medical researchers of the disciplines concerned to be active.

5.2.3 Arteriosclerosis

As regards morbidity and mortality, *arteriosclerosis with its secondary diseases* (angina pectoris, myocardiac infarction, stroke etc.) *stands at the head of all diseases in modern industrial states* [380]. Combat of it is one of the most important medical problems of our time. The reason why we discuss arteriosclerosis here is that it also decisively contributes to the genesis of most of the other O_2 deficiency conditions and diseases discussed. The tumescence of the arterial vessel wall cells, characteristic of early arteriosclerotic changes and the relevant noxae, have been discussed in Paragraph 1.1.1. It is claimed, not injustifiably, that the human is as old as the condition of his vascular system, and the topography of this condition determines how well or how poorly the individual organs of the organism are perfused with blood and supplied with oxygen (energy).

The *prophylactic combat of arteriosclerosis* is one of the main tasks of preventive medicine, for it shows no symptoms in its early phases and when pathologic signs are recognized in its advanced stage, it is usually too late for therapy because the changes are irreversible.

Arteriosclerosis is an O_2 deficiency disease in which the drop in the $P_{O_{2\text{-}art}}$ (e.g. hitherto age-conditioned) *leads directly to a weakening of the O_2 metabolism in the endangered tissue area* (walls and ramification points of the arterial blood vessels), *and in which, therefore, no "protection" is afforded by the saturation character of the upper part of the HbO_2 dissociation curve* (cf. Fig. **124** above). *Conversely, the same reasons lead us to expect particularly positive prophylactic effects if the $P_{O_{2\text{-}art}}$, at rest, is kept at high levels over many years by regular, strength-requiring exercise training (e.g. certain sports, mountain inhabitants, home trainers), or if an already considerably reduced $P_{O_{2\text{-}art}}$ is permanently raised again to levels that existed in the best years of youth, by means of several variants of the O_2MT* (see Paragraph 4.).

The methodological basis of this kind of *prophylaxis* of arteriosclerosis is the numerical calculation of the P_{O_2} in the interior of the arterial vessel walls, according to the *two-dimensional diffusion equation* shown in Fig. **243**. The calculation showed that the O_2 supply to the middle of the vessel wall by diffusion from the lumen reaches critically low levels when the resting $P_{O_{2\text{-}art}}$ drops below 75–80 mmHg (10–10.7 kPa). This resulted in the idea that the sclerotic degeneration of the arterial vessel walls can be the better delayed, the better the $P_{O_{2\text{-}art}}$ can be kept by O_2MT with as few interruptions as possible at levels above 75–80 mmHg from an age of about 50–60 years. The O_2MT concept is still young, and the timespan for the observation of prophylactic effects is certainly decades in the case of arteriosclerosis. The only volunteer who has lived over approximately 15 years (from the age of 65 to 81) almost uninter-

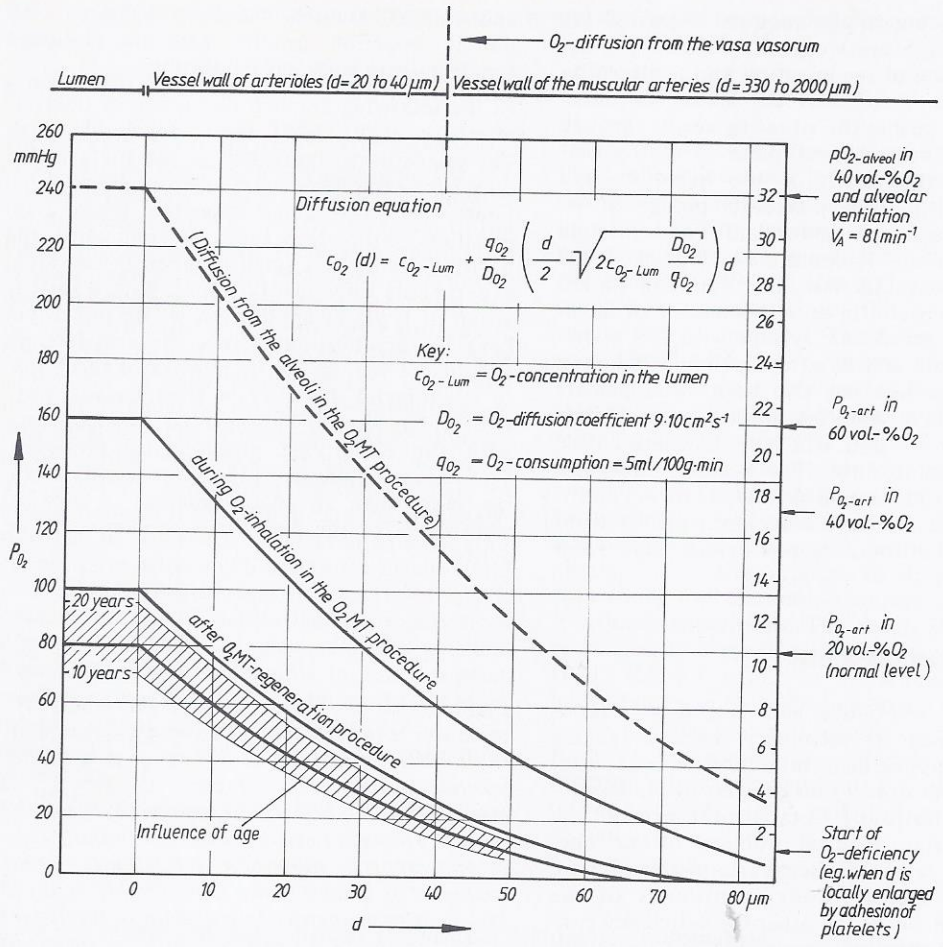


Fig. **243** Quantitative presentation of the very great increase in the P_{O_2} produced in the lumen of the arterial vessel wall, by means of increase in the O_2 proportion in the inhalation air from 20 vol.-% (normal level) to 40 or 60 vol.-%. A. and M. von Ardenne 1977, unpublished. Result: O_2 deficiency favored in a priori thickened arterial wall areas or those narrowed by clinging blood constituents. Conclusion: maintenance of $P_{O_{2\text{-art}}}$ levels, measured at rest, around or above 80 mmHg (10.6 kPa) for decades

ruptedly with levels of the $P_{O_{2\text{-art}}}$, at rest, above 80 mmHg (10.7 kPa), is the author. Perhaps the measurement in Fig. **212** A (see Paragraph 3.4.4), which allows us to conclude that his vascular system is in an extraordinarily good condition, is a first indication of the *success of arteriosclerosis prophylaxis by the utilization of the O_2MT over decades*. The following finding indicates that this assessment is very probably true: it was possible to normalize the blood pressure to a considerable extent in almost all hypertensive patients with not yet chronic high values, by means of the high-charging of the O_2 status (especially of the $P_{O_{2\text{-art}}}$) with few interruptions over many years, using the O_2MT variants GK 4-I or GK 2-I. Blood pressure reducing substances were given adjuvantly in strongly reduced doses.

By arteriosclerosis we understand a disease of the arteries which involves changes, particularly thickening and finally hardening, in the vessel wall. The disease begins insidiously (cf. Fig. **236**), the pathological process not being accompanied by pain or typical symptoms. It is not usually until the late stage, when the defective texture of the vessel wall layers is irreversibly established, especially at the ramifications, that

Table **37** Measurements on dysregulated hypotensives before and after the 36 h O_2 multistep therapy procedure, variant GK 4-I (cure-like application; duration of each session 2–8 h; always combined with standard medication; repetition on consecutive days)

No.	Patient Name	Sex	Age years	Σt-O_2MT total number of hours	arterial resting P_{O_2} (mmHg) before therapy	after therapy	mean blood pressue (mmHg) before therapy	after therapy	Remarks
1	H.B.	♂	39	10 (with nicotinic acid)	—	—	105/75	125/75	
2	R.W.	♂	63	20	62	75	100/60	125/85	chain smoker
3	M.Ch.	♀	57	20	85	93	100/65	120/75	
4	R.J.	♀	52	20	85	95	105/70	120/85	
5	G.R.	♂	37	30	87	96	105/60	125/80	
6	K.Ch.	♂	34	30	81	89	105/70	125/80	
7	F.B.	♀	30	30	84	96	115/75	135/85	
8	B.G.	♂	48	30	70	90	110/65	125/80	
9	K.G.	♂	46	30	86	92	95/65	115/80	
10	G.W.	♂	58	30	75	92	95/70	110/80	
11	S.B.	♀	60	30	70	98	95/65	125/80	
12									
13	S.S.	♂	44	(1 year intensive exercise training)	(79)	(100)	105/75	125/75	for comparison

the feeling of great well-being which normally sets in a few hours after therapy, *greater exertions should be avoided in the first few days*, until the lasting increase in blood pressure amplitude has caused the formation of new cellular and energetic reserves.

When the blood pressure amplitude is permanently raised to over 200% in a relatively short time, as in Fig. **246**, and the $P_{O_{2\text{-art}}}$ is also rapidly increased, this is a *far-reaching change in the whole organism*. The patient's organs and tissues had, usually over many years, adapted themselves to the poor circulation by means of a more economic microtopography of vascularization and cell population in the intercapillary space, and then, suddenly, this excess – and that permanently! It would be a rewarding task to investigate the effects that such a rapid increase in blood pressure amplitude has on the various organs and tissues (increased mean tissue P_{O_2}, reduction of pathogenetic factors). Individual observations of the alleviation of senile diabetes, reimplantation of loose teeth, the reduction of heart complaints etc. should make us thoughtful. It can be seen for the whole person that, after the lasting doubling of the blood pressure amplitude in older people who have suffered from hypotension for many years, their strain capacity, their energy and their mental performance capacity are greatly increased, i.e. their *vitality is significantly increased.*

Further investigation taught us that blood pressure and its amplitude could also be raised in patients with regulatorily conditioned hypotension with the GK 4-I therapy variant. Measurements of the results with this less intensive (milder), but therefore more time-consuming variant are compiled in Table **37**.

5.2.5 Hypertension

We were stimulated to try to combat hypertension using O_2MT by a significant, basic physiological fact, i.e. that virtually the full level of the $P_{O_{2\text{-art}}}$ is effective for the stimulation of O_2 metabolism in the vessel walls of the arteries and arterioles, and this arterial oxygen partial pressure is extremely strongly increased during the O_2MT procedures (cf. Fig. 7) and afterwards is usually significantly raised on a permanent basis. Hypertension is the sclerogenous noxa with which, using experiments on laboratory animals, the non-specific mesenchyme reaction was found and the fast mesenchyme incorporation into the wall of the arteries examined [172, 194] (cf. Fig. **113**). In the experiments on rats, acute arterial hypertension was artificially brought about by the subcutaneous injection of 1.2 mg hypertensin. It is known that hypertension in humans (diastolic blood pressure > 95 mmHg (12.7 kPa)

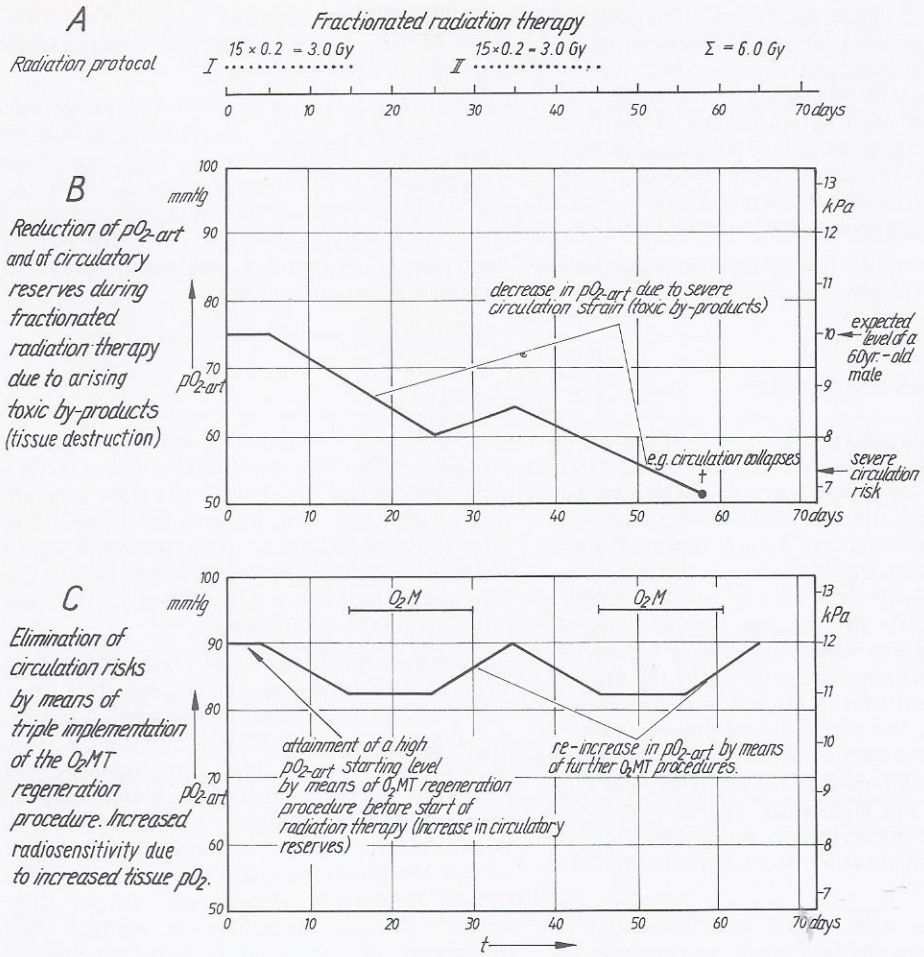


Fig. 249 Schematic presentation of the course of the arterial P_{O_2} during conventional fractionated radiation therapy of the lung carcinoma (A), in the type of treatment usual today (B) and in a new of treatment with triple implementation of the O_2MT (C)

5.3 Combat of oxygen deficiency diseases

5.3.1 Conditioning by slow increase in exertion, increase in mobility and CO detoxification

It is frequently necessary or advisable to *prepare the patients* before or at the start of O_2MT, in order to increase their stress capacity and their mobility, and to optimize O_2 transport to the tissue via the bloodstream. The observation that the physical strain capacity rises quickly under O_2 application (cf. Figs **89**, **125**, **224**) makes it possible to condition weakened patients for O_2MT variants which would normally be contraindicated (variants GK 1, GK 2-III, GK 4-II with Alupent) by the careful increase in exertion at the start of the procedure (under medical supervision). This conditioning with O_2 is of great significance in the O_2MT obstetrics procedure, GK 2-IV.

A certain mobility is a prerequisite for the variants of the GK 2 group. It is often possible to produce sufficient mobility in physically disabled patients by means of the classical

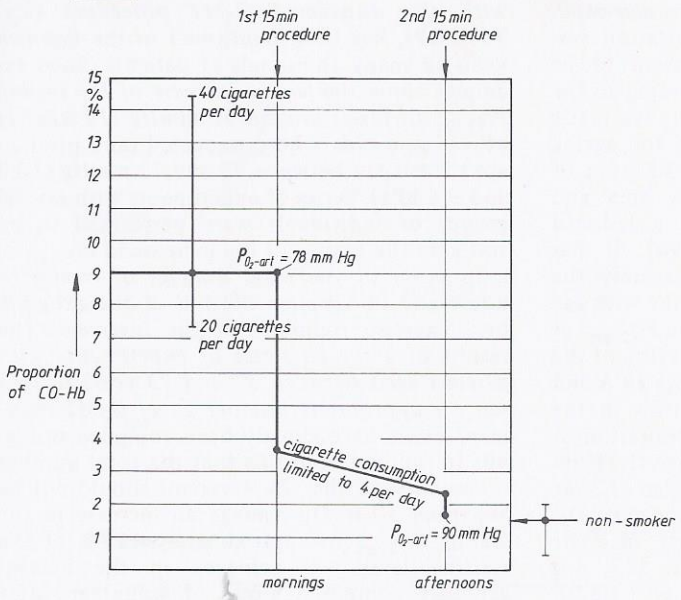


Fig. **250** Detoxication of hemoglobin in carbon monooxide poisoning by means of two 15 min O_2MT quick procedure GK 2-I. Guiding levels

cures, mentioned in Paragraph 5.1.9. We should also think of *preprocedures with special drugs*. An example here is the successful treatment of chronic polyarthritis using s.c. applied interferon-γ, according to Obert and Hofschneider [392].

For patients damaged by chain-smoking or car exhaust fumes, conditioning by carbon monoxide detoxification is desirable. The CO poisoning of the hemoglobin leads to a reduction in the O_2 transportation capacity of the blood. The poisoning causes a reduction in the $P_{O_2\text{-art}}$, at rest, in the HbO_2 saturation, or the O_2 uptake of the organism, i.e. a deterioration in the O_2 status. In persons damaged by chain-smoking or car exhaust fumes, up to 15% of the hemoglobin can be excluded long term from the O_2 transport. The consequence is a critical deterioration in the O_2 supply of the organism. In chain-smokers consuming daily 20–40 cigarettes, we measured a fraction of 7.5–14.5% CO-Hb, using a Corning 2500 CO Oximeter (Corning Medical, Fernwald, FRG). The high poisoning quotas named, along with other overlapping harmful factors (cigarette paper, nicotine, bronchitis due to inhalation of smoke), explain some of the difficulties that limit the improvement of the P_{O_2} levels by O_2MT specifically in chain smokers.

In the situation described it was important to find as simple a way as possible for detoxification. Detoxification in clinics has so far been undertaken in usually very costly hyperbaric chambers or with special pressure masks (e.g. hyperbaric oxygen mask from Ortho-Med Ltd, Edinburgh, GB) using O_2 with approximately one half atmosphere positive pressure, for at least 1 hour. Detoxification by means of two 15-min O_2MT quick procedures GK 2-I, shown in Fig. **250**, is simpler and less costly in terms of time and expense. It is only necessary to perform a fast detoxication in wards for hyperbaric oxygen for patients who cannot cope with exertion or who are disabled. As the figure shows, the fraction of CO-Hb drops from 9% after the first 15-min O_2MT quick procedure and, after restriction of cigarette consumption to 4 per day, to 2.3%. After a repetition of the 15-min O_2MT quick procedure with its high O_2 flow and its highly charged blood microcirculation, the CO-Hb falls to 1.5%, i.e. to levels that are, on average, found in nonsmokers. At the same it is sensible to convince such patients, by demonstrating data like those in our figure, of how greatly their O_2 status, i.e. their energetic status, can be raised by restricting their cigarette consumption.

not yet irreversible eye damage. Thus, for example, patients often reported the disappearance of the initial stages of cataract after O_2MT. In extensive discussions on the causes of cataract [184], the drop in the $P_{O_{2\text{-art}}}$ in old age is not usually mentioned.

Ophthalmology has the advantage that optical observations of the eye-ground can immediately recognize changes in the vessel system, for example. It is therefore of pioneering significance that ophthalmology, after earlier doubts (see here also Paragraph 5.3.3, nicotinic acid), now admits and even utilizes the *possibility of vasodilation by means of specific drugs, even for the brain and the ocular system attached to it* [185].

As long as no irreversible damage to the optic nerve fibers and retina cells has occurred, a relatively slight increase in the O_2 status (restoration of a reduced $P_{O_{2\text{-art}}}$ at rest, Fig. **251**) and in the η-value are often sufficient to transform the diminished metabolism back to full function. The 80 min O_2MT nicotinic acid procedure, KA 1 variant (cf. Table **32**) should be seen as particularly suited for this. Great therapeutic, long-lasting effects have also been found after the application of the 36 h O_2MT variant GK 4-I and the 15 min O_2MT quick procedure, GK 2-I variant (cf. Tables **27** and **25**). There are already many impressive individual observations of an improvement in retinal circulatory disorders in older patients (e.g. 73-year-old male, $P_{O_{2\text{-art}}}$, at rest, raised from 72 to approximately 90 mmHg) and also of the elimination of visual field defects and of sudden changes in visual acuity. The administration of Pentoxifyllin (Trental, Trental 400) both i.v. and orally [413] has proved its worth as an adjuvant step to improve blood supply of the retina. The case of a female patient who was extremely light sensitive, always had to wear dark glasses and could no longer watch television, was particularly impressive. The high degree of light sensitivity disappeared immediately after completion of the O_2MT procedure. She no longer needed her dark glasses and could once more watch television regularly. In another case (Krutoff, Munich, FRG), an 84-year-old patient reported that for some time he had only been able to read if he used glasses and a magnifying glass at the same time. After the O_2MT cure he could read using a pair of glasses that he had laid aside 10 years before. The optical data that had existed for him 10 years previously had returned. There are several other examples along these lines where new glasses became necessary after O_2MT and, to the amazement of the optician, lenses with less refraction were again sufficient. There were reports by Meixner (Villingen, FRG) of some cases of elimination of glaucoma by means of normobaric O_2MT. Observations on the reduction in intraocular pressure due to the treatment in the hyperbaric chamber or with O_2 application at a flow rate of 15 l/min [414] make the application of the O_2MT excess pressure quick procedure, GK 7 variant, seem to be strongly indicated against glaucoma. These experimental observations carry great weight because they prove the reversible character of this type of eye disease caused by oxygen deficiency.

g-Strophanthin is often included in the drug combination to alleviate ocular O_2 deficiency. That this cardiac glycoside, in addition to its main effect on the myocardium, also has a peripheral effect and, more than anything, positively influences the cerebral metabolism, is emphasized in [185] and [418]. It was proved in [186] with radioisotope angiography in animal experiments that the glucose concentration increases in all examined parts of the brain under the influence of g-strophanthin. More importantly, it has recently been proven using the Xenon clearance method that in both deficiently and sufficiently supplied brain tissue, the circulation is significantly improved even when there is no manifest cardiac decompensation. From the viewpoint of these experimental findings, the results discussed in Paragraph 2.2.1 [148, 420] of the reliable effect of perlingually administered g-strophanthin, are of great relevance and interest.

The practice and utilization of the O_2MT in ophthalmology have begun. Measurements of the (lasting) influencing of critical flicker fusion have been initiated. After the good results obtained in our Institute and by many O_2MT partners, this field of application is indisputably a rewarding one. It is therefore advisable to establish contacts with ophthalmologists in order to arrange the continuous admission of respective patients to specialized O_2MT cure institutes, in order broadly to substantiate the promising individual observations made so far.

O_2 deficiency of the ear. O_2 deficiency is also frequently the primary cause of *severe hearing defects*. A well-known example of this is the *Ménière's disease* [415] which, if it occurs repeatedly, often leads to a loss of hearing in the right ear. A Ménière attack, which is characterized by severe labyrinthine vertigo which does not usually subside for several hours, is often triggered when hypotensives experience phases with particularly low blood pressure and (or) O_2 status. We already have experience of

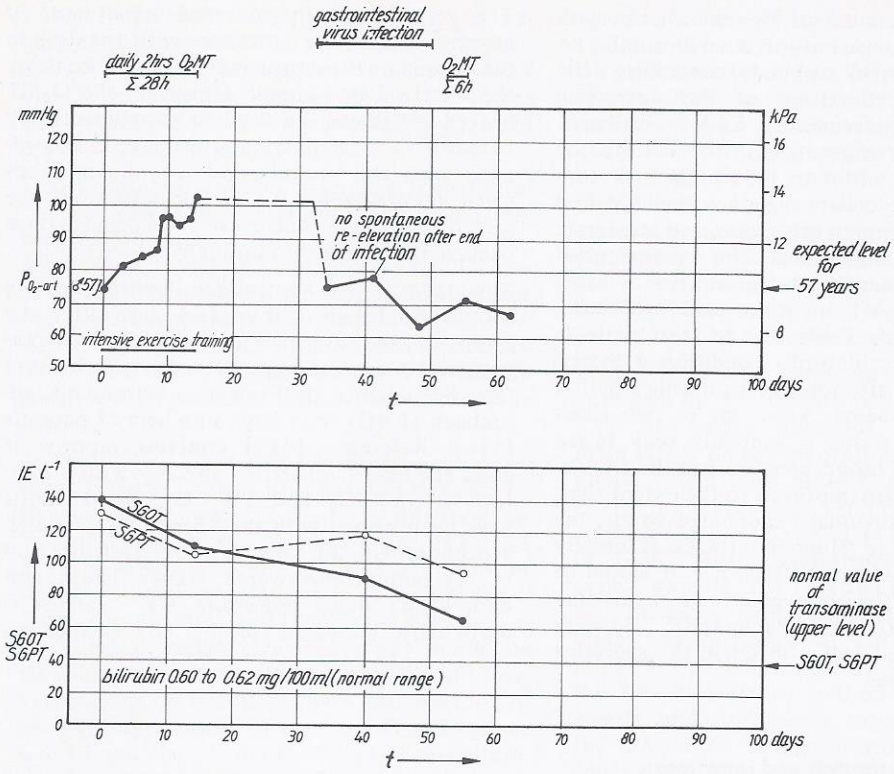


Fig. **257** Change in the arterial P_{O_2} (above) and improvement in the transaminase levels (below) by the ambulant O_2MT treatment (variant GK 4-I, 2 h per day) of a patient with progredient chronic hepatitis. Initially positive treatment interrupted by virus infection

5.3.6 Kidney

The O_2MT should be able to help in the kidney area, particularly by means of its antiarteriosclerotic components. It is known that repeated long-term periods of hypertension regularly lead to *arteriosclerotic alterations in the kidney.* The vasa afferentia are the most affected, the lumen being increasingly constricted by the incorporation of mesenchyme in the vessel wall. Secondarily, the glomeruli sclerose and the affiliated renal tubuli atrophy. The mentioned constriction of the lumen soon leads to a drop in circulation of the kidney. As this procedure progresses the amount of filtrate gradually falls with the increasing failure of the glomeruli, and the blood flow of the kidney deteriorates further. Thus a feedback system presents itself, in which the reduction in renal circulation and the atrophy of the parenchyme in turn lead to hypertension, or intensify it. This feedback mechanism should mean that the *affected kidney contributes to the fixation of hypertension.* If this process is very pronounced, it results in cirrhosis of the kidney. These specific connections endow the early combat of irreversible degeneration of arterial branches and arterioles in the vascular kidney with particular importance. Due to the feedback mechanism mentioned, the analysis of the kidney function is a good indicator of the stage of the hypertension.

In relative rare cases disorders of the kidney function are the primary cause of hypertension. Clinical experience with the prophylactic and therapeutic application of O_2MT indicate that the probability of kidney damage caused by incoming toxins can be considerably reduced if the O_2 status is maintained at a high level, over long periods of time with few interruptions.

5.3.7 Pancreas

It is known that the proteohormone insulin is formed in the β-cells of the islets of Langerhans in the pancreas, a process that is apparently very sensitive to O_2 deficiency. This can be concluded from the increase in the frequency of diabetes mellitus with advancing age, which roughly correlates with the drop in cardiopulmonal performance, or in the O_2 uptake, at rest. However, in senile diabetes the average O_2 metabolism does not drop below the conservation metabolism, for the decline in insulin production is of reversible character in the first few years after the onset of senile diabetes at least. Thus it has been known for improvements in senile diabetes to occur with the transitions to a changed lifestyle with energy-demanding exercise training. A *very significant drop in post-therapy blood sugar levels could almost always be observed in senile diabetics after the* O_2MT (partly influenced by more effective glucose catabolism). The improvement was often so great that just a light diet was enough to keep the blood sugar sufficiently low. Several cases have been reported to us in Dresden of insulin-dependent diabetics between the ages of 50–70 years, who had to reduce their insulin dose significantly after O_2MT in order to avoid hypoglycemic episodes. In one case (reported by Skeiner, Puch, Austria) the patient could switch to oral antidiabetics and finally come off these too.

In several cases with so-called chronic pancreatides a normalization of the amylase levels in blood was observed after the procedure. Strict fasting with the breakdown of protein stores [233] also causes a decline in senile diabetes (cf. Fig. **265**), a further indication of the synergistic effect of fasting.

5.3.8 Myocardium

In the *myocardium* there are specific conditions for the supply of O_2 (cf. also Fig. **93** above). The normal mean $P_{O_{2\text{-ven}}}$ is approximately 17 mmHg (2.3 kPa). Circulation and O_2 consumption are not constant. *The temporal course of the mean* P_{O_2} *in the heart muscle during hard physical labor* is shown in Fig. **258**, on the basis of calculations by Thews. In the systole the circulation in the inner layers of the left ventricle temporarily stops completely, for mechanical-vascular reasons. The integral P_{O_2} here has the lowest level of all healthy tissue in the organism. On the other hand, the systole has the highest O_2 consumption. The inner layers of the left ventricle are therefore the area most threatened by oxygen deficiency.

The myocardium, with the combat of its insufficiencies and diseases, is one of the main

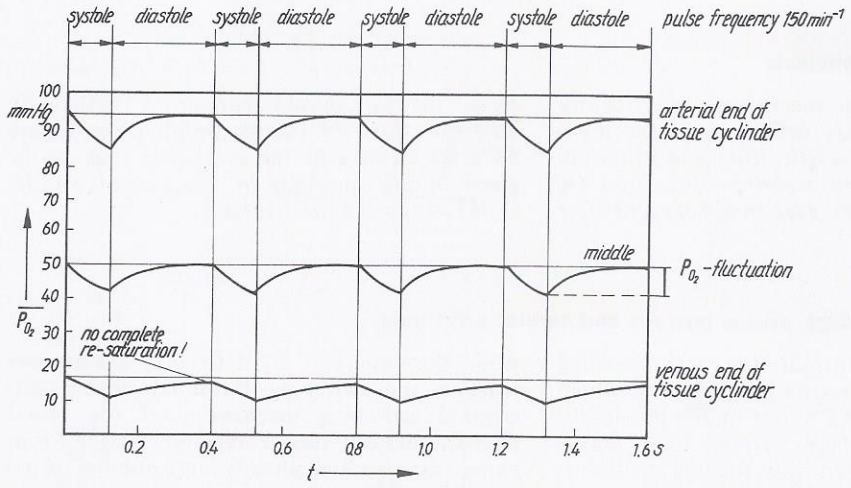


Fig. **258** Temporal change in the mean P_{O_2} of the heart muscle in three different areas of the tissue cylinder during heavy physical labour; modified according to G. Thews [420]; 1 mmHg = $1.33 \cdot 10^2$ Pa

domains of O_2MT research. This is partly a consequence of the fact that the results of our work on the development of the cancer multistep therapy, with its selective triggering of irreversible hemostasis in the cancer tissue, also helps, or can also help, in the combat of the myocardiac infarction because the same mechanism of vascular occlusion is brought about here as occurs naturally during the infarction [366]. Various results, immediately utilizable for the patients, are now open to cardiologists: they range from prevention, through prophylaxis and therapy, to rehabilitation. It is now vital that the responsible medical practitioners read – with great sobriety and objectivity – the original papers, partially coauthored with Reitnauer [e.g. 111, 122, 146, 148, 150, 171, 198, 199, 338, 366] and also the sections of this book dealing with this subject. It is composed of measured results, experimental findings, clinical experiences, methodological studies but also of speculative ideas and working hypotheses of our small Dresden research group, all of which are in need of verification, confirmation and comprehension. In this time of a flood of information, the gaining of many active cohelpers and cochampions, not only within the group of friends of the "Gesellschaft für Infarktbekämpfung" in Schorndorf-Haubersbronn (FRG) is necessary for the further success of our movement. The author relies here on the younger generation, who have the mental energy, despite the daily hectic pace in hospitals, to become accustomed to thought processes which cannot, or cannot yet, be found in official textbooks. The following paragraphs aim to give a survey of our conclusions from our own work and from sports medicine, which is close to us, under the aspect of making them quickly utilizable for the patient.

5.3.8.1 Infarct prevention

We can expect a great contribution to *infarct prevention* and to the prevention of respective prestages such as angina pectoris, arrhythmias and other cardiac insufficiencies of varying kinds, *from a prophylaxis of arteriosclerosis*. We have already explained elsewhere (see Paragraphs 3.4.4, 5.2.1, Figs **212** and **243**) our idea that arteriosclerotic degeneration of the arterial vessel wall can be delayed if, by using the O_2MT, the resting $P_{O_{2\text{-art}}}$ is maintained as continuously as possible at levels above 75–80 mmHg (10–10.7 kPa) from the age of 60–70 years onwards. The transcutaneous P_{O_2} measurement after blood compression and release in a volunteer who had used the O_2MT for 15 years, shown in Fig. **212** A, is a first indication that a prophylaxis of arteriosclerosis succeeds, or can succeed, in this concrete way.

A further contribution to infarct prevention arises from sports medicine, by which the drop in COP with advancing age (cf. Figs **66**, **68** and **153**) is countered by *daily exercise training* (e.g. 10 min minimal training with raising of pulse rate to 180 – age, see Paragraph 1.1.9.5).

5.3.8.2 Infarct prophylaxis

Since the infarction mechanism is evidently released when the O_2 deficiency in the myocardium exceeds a certain level and duration, *the maintenance and securing of a good O_2 status with few lapses, even in old age and after severe distress*, should represent a particularly effective form of infarct prophylaxis. Figure **66** gives an idea of the great help that can be given in this question by the variants of the O_2MT, discussed in Chapter 4.

5.3.8.3 Preinfarct stage, angina pectoris and cardiac arrythmia

Infarct prophylaxis includes the careful heeding and combat of the warning signals with which Nature generally gives notice of the possibility of an infarction. These warning signs, which must be taken very seriously, include the occurrence of cardiac arrhythmias and, most importantly, attacks of *angina pectoris*. According to our concept, angina pectoris attacks occur when the extent of O_2 deficiency has not yet reached the switching threshold of our discovered switching mechanism of the blood microcirculation (see Paragraph 1.1.1). From experiences with an already large number of patients with cardiac insufficiency we can state with certainty that, in a very high percentage of cases, angina pectoris complaints and also the

occurrence of cardiac arrhythmias are repressed in terms of frequency and severity, if not even eliminated, by O_2MT variants adapted to the individual case. Cases have been reported of heart patients who were faced with the prospect of bypass operations, but who first underwent an O_2MT procedure. All cardiac complaints and also ECG anomalies disappeared. They could be spared the operation. A large number of findings were observed or reported in which cardially conditioned breathing difficulties or anginal complaints disappeared in physical exertion.

A further, simultaneous method of combatting angina pectoris is either the application of a stomach-resistant strophanthin preparation (Strodival mr) on the basis of a cure or the *ad hoc application* of the *Strodival special preparation*, developed in conjunction with the author, dealt with in more detail in the following paragraph. Dohrmann [147] reports on the arrest of angina pectoris attacks in 85% of cases within approximately 8 min after the perlingual administration of this preparation.

There are reports on an extensive reduction of deaths due to infarction in underground mining by means of immediate treatment with perlingually administered g-strophanthin (e.g. Strodival special) in anginal complaints [421]. Under otherwise identical conditions and with roughly the same number of heart attacks (around 250), 11 deaths occurred without immediate Strodival therapy, and none with this prophylaxis.

5.3.8.4 Infarct mechanism

Primarily as a result of Reitnauer's experimental skill we have gained deep insight into pathophysiological processes of the myocardiac infarction and its combat, from micro pH measurements on pulsating rat hearts (cf. Fig. **105**) with artificial triggering of infarct (cf. Fig. **106**), with controlled termination of the O_2-deficient phase (cf. Fig. **107**) and with administration of g-strophanthin (cf. Fig. **84**). Further decisive aspects of the mechanism ensued from several years of our research into the details in the selective triggering of hemostasis in the cancer tissue by optimized over-acidification of the tissue plus synergistically acting hyperthermia.

On the basis of the well-known processes in the myocardium, described in Figs **258** and **259**, our insights were particularly deepened by the pH measurements in the myocardium (Fig. **260**), the analysis of the consequences of the drop in pH occurring in the O_2-deficient infarcted volumes, in accordance with Table **39**, and the survey of main influences, compiled in Table **40**. The pH measurements in Figs **84** and **107**, and the measurements of P_{O_2} and micro-

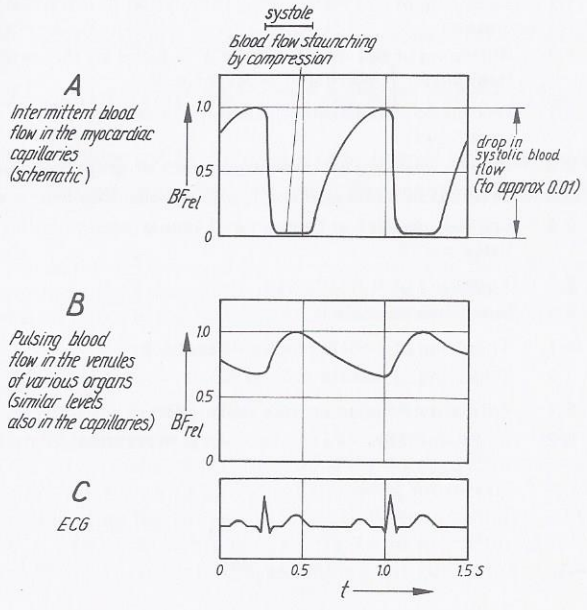


Fig. **259** Periodic blood flow reduction due to vascular compression in the myocardium during the systole of approximately 0.3 s duration (A). The specific hemodynamics renders the myocardium greatly sensitive towards triggering of stases, compared with other organs (B)

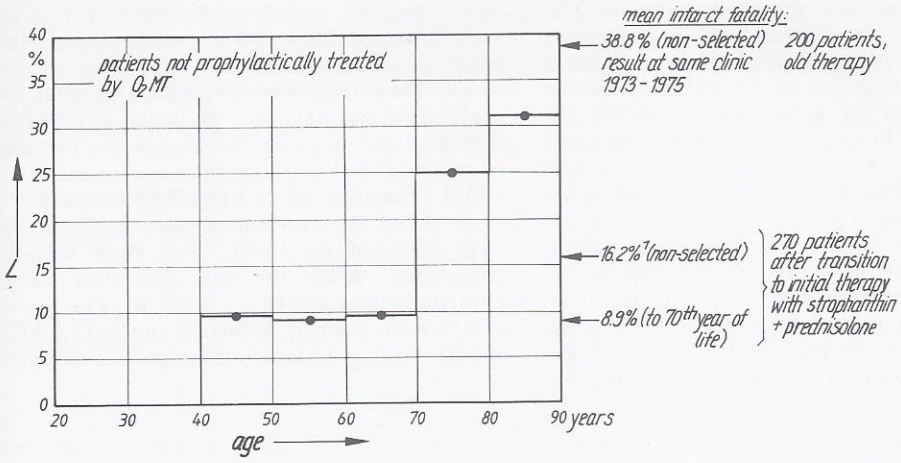


Fig. **262** Indication of the increasing fatality of cardiac infarcts with decreasing arterial P_{O_2} (increasing age). Results of initial therapy of infarct patients with the combination of g-strophanthin + prednisolone suggested in [144], in the Waldkrankenhaus Berlin-Spandau (R. E. Dohrmann et al. [152])

[1] In a multicentric WHO study with 7738 patients (Europe, old therapy) the mean fatality of infarcts for 1977 was given as 40% (non-selected)

5.3.8.6 Clinical infarct therapy

The three different treatment phases in the combat of acute myocardiac infarction have already been defined and described in Table 8. Immediate therapy in the reversible phase (emergency situation in approximately the first 20 min after onset) has been discussed in the previous paragraph. With therapy in the clinic in the subsequent irreversible phase we distinguish, on the basis of Fig. **116**, between clinical therapy *before* occurrence of the cytolytic chain reaction (time-span 20 to approximately 120 min) and clinical therapy *after* occurrence of the cytolytic chain reaction (time-span from approximately 120 min to approximately 2 days). High dosage α-methyl prednisolone (von Ardenne and Kern [144]) is used to inhibit the lysosomal cytolytic chain reaction by stabilizing the lysosomal membranes. It has already been mentioned above that Dohrmann achieved a reduction in infarct lethality from 38 to below 16% in the treatment of 270 nonselected infarct patients with this combination in his clinic in Spandau (Berlin West) [152, 153].

If the infarction mechanism has entered its irreversible stage, which can no longer be significantly influenced, the *chances of survival depend greatly on the current O_2 status of the patient*. This is indicated by the clinical findings analysed in Fig. **262**, according to [152]. Persons with an increased risk of infarct (old age, warning signs, unfavorable P_{O_2} values) should therefore do everything to improve their O_2 status as much as possible by adapted variants of the O_2MT.

5.3.8.7 Infarct rehabilitation

A considerable increase in the patient's capacity for exercise occurs even during implementation of the 36 h (18 day) O_2MT procedure GK 4-I, in correlation with the rise in the arteriovenous P_{O_2} difference measured without O_2 inhalation. This rapid increase in capacity for exercise is of great significance for rehabilitation after a myocardiac infarction, where the treatment has so far trodden a tightrope between the triggering of a further infarct with too much exertion and the unnecessarily long return to a normal lifestyle, adapted to the case, with too little. This former tightrope is made very much wider and thus the patient risk significantly reduced by the "initial mobilization" of the infarct patients, occurring after the first sessions of the

O_2MT treatment, as in examples in Fig. 89. The mobilization effect of the O_2MT thus signifies a decisive aid to patient rehabilitation after myocardiac infarction, an aid which should be quickly grasped by all centers responsible for this problem. In order to make this demand more understandable and acceptable we will give here the observations in a typical individual case: a middle-aged patient comes to us in Dresden soon after suffering a myocardiac infarction, to undergo an O_2MT cure. On the day of his arrival a low level of the $P_{O_2\text{-art}}$ is measured and he can only climb to the second floor of his 13-storey hotel because severe anginal complaints prevent him from climbing further. We categorize him as "physically disabled". After just 12 hours of the O_2MT treatment cycle this physical disability vanishes and the patient climbs the 13 storeys of his hotel without the reoccurrence of anginal complaints. The "initial mobilization" has now put him in the position to perform the obligatory exercise of our 36 h O_2MT procedure GK 4-I regularly between sessions. After the cure the patient climbs to the 13th floor of his hotel twice more without complaints. After the cure and even weeks afterwards measurements show his $P_{O_2\text{-art}}$, at rest to have risen by about 20 mmHg (2.7 kPa) and his $P_{O_2\text{-ven}}$, at rest, to have greatly dropped.

5.3.9 Vascular system. Fasting as a further step of therapy

The arterial side of the blood vessel system, on whose functioning ability so much depends for human health and life, is a main target area of the O_2MT. The various *types of blood vessels* and some of their data are compiled in Table 41. The most important disease of the blood vessel system, arteriosclerosis, and therapeutic measures to combat it using O_2MT have been discussed in Paragraphs 3.4.4 and 5.2.2. We will therefore only supplement this here with a few physiological considerations.

The *inter-relationships between causes and effects in the genesis of arteriosclerosis* are shown schematically in Fig. 263. Sclerogenous

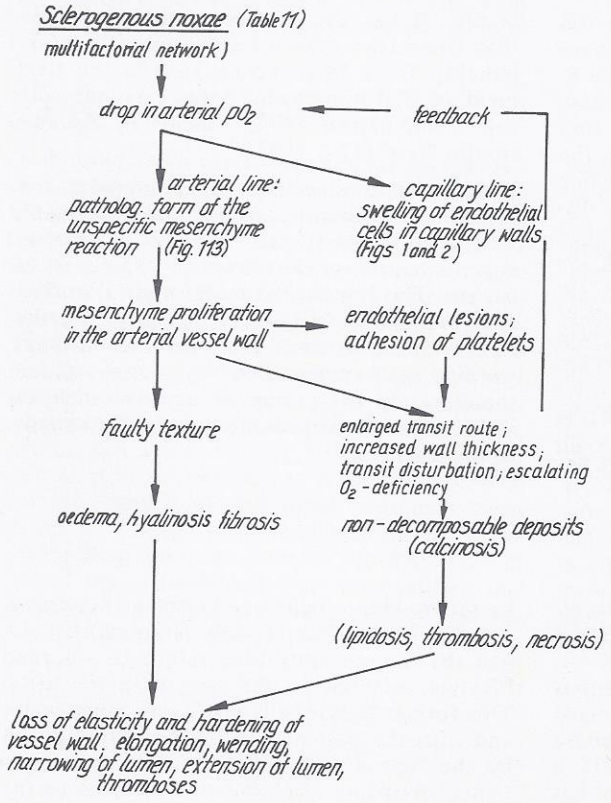


Fig. 263 Schematic presentation of the interrelationships between causes and effects in the emergence of arteriosclerosis; according to [381] with modifications

Table 41 Diameter and wall thickness as well as relationships between wall thickness and inner radius for varying contraction conditions of the smooth musculature in the different vessel types of the human organism. By aggregation and attachment of platelets at injured sites of arterial vessels, a critical increase of the "effective wall thickness" can occur, which is decisive for regular supply [383]

Type of blood vessel	Ø range µm	Vasomotor activity	Thickness Inner radius	Wall thickness range µm	Portion of major components endo-thel.	elast. fibres	muscle fibres	collag. fibres
1. elastic artery	20 000 to 10 000	–	1:6 (1:5 to 1:7)	3300 to 1700	small	very big	medium	big
2. muscular artery	10 000 to 1000	relaxed	1:5	2000 to 330	small	big	big	medium
		contracted	1:3					
3. arteriole	200 to 20	relaxed	1:5	40 to 20	small	medium	very big	medium
		contracted	1:1					
4. capillary	7 to 5	–	1:7.5 (1:5 to 1:10)	0.7 to 0.9 (to 2.5 in diabetic protein depositing)	very big	nil	nil	very small
5. venule	20 to 500	relaxed	1:12.5 (1:10 to 1:15)	1.6 to 40	small	small	big	small
		contracted	1:8.5 (1:7 to 1:10)					
6. medium vein	1500 to 15 000	relaxed	1:12.5 (1:10 to 1:15)	120 to 1800	small	medium	big	medium
		contracted	1:8.5 (1:7 to 1:10)					
7. large vein	15 000 to 30 000	–	1:12.5 (1:10 to 1:15)	1200 to 2400	small	medium	medium	very big

noxae, of which O_2 deficiency is one – or, rather, which cause nearly all O_2 deficiency (see measurements in Paragraphs 1.1.8.3 and 1.1.9.3) – *trigger the swelling of endothelial cells in the capillaries, thus reducing their cross-section, and also the initially reversible incorporation of mesenchyme in the arterial vessel walls*. An increase in peripheral resistance is observed here as the direct response. The incorporation of mesenchyme into the arterial vessel walls, which is based on the unspecific mesenchyme reaction [172, 194], leads in particular to thrombocytes being strongly attached [383] with critical changes in the vascular lumen and, if the changes persist, to a loss of elasticity, among other things, and also a hardening of the vessel wall as a result of deposits.

These changes are often localized at ramifications where, according to [173], *turbulences in the bloodstream* occur. These turbulences, in addition to mechanical effects (e.g. lesions), probably cause a *local adherence of platelets and a reduction in the O_2 supply to the vessel wall*.

It was explained above that there are probably *two stable states* locally in the walls of the muscular arteries and the arterioles: condition A with a small wall thickness (normal state) and condition B with critically increased wall thickness (pathological state). Paragraph 5.2.2 also discussed the fact that the intensive temporary raising of the O_2 metabolism in the critical area of the vessel wall can cause state B to change to the positive state A.

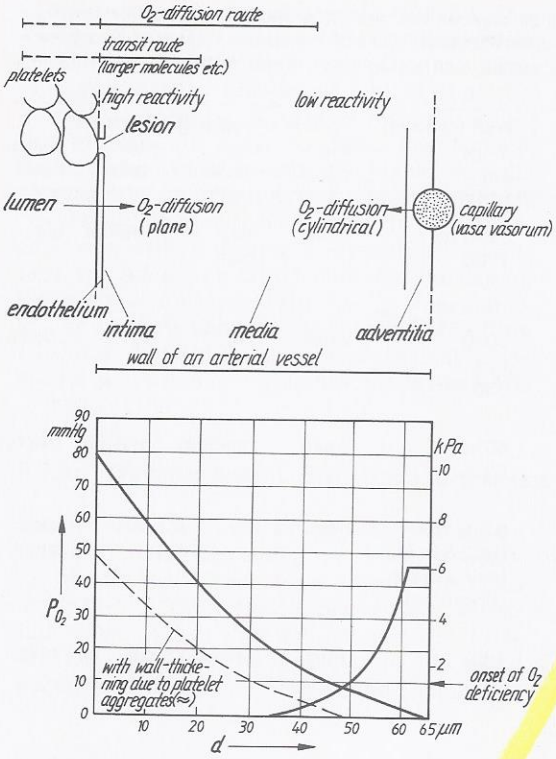


Fig. **264** O_2 supply to the arterial wall by diffusion from the lumen (plane-symmetric) and from the vasa vasorum (cylindrical-symmetric). For calculation see Fig. **243**

On the subject of this change, which can last for months or years, Fig. **243** shows a quantitative presentation of the P_{O_2} distribution in the vessel wall under the given margins, calculated with the aid of the "*diffusion equation for the case of planar interfaces*". It gives exact information on how greatly the $P_{O_2\text{-art}}$, and hence also the P_{O_2} level in the critical wall areas of the arterial vessels, can be increased by the doubling or trebling of the O_2 proportion in the inhalation air. Like the further presentation in Fig. **264**, this calculation reveals the *dominant role of the O_2 diffusion (plane diffusion) from the lumen with its high P_{O_2} level, to the critical areas of intima and media.* The calculation also shows us that the direct O_2 diffusion from the lumen is enough to supply the healthy arterioles with the greatest wall thickness (d = 40 µm) sufficiently with oxygen. But both presentations also show how greatly the O_2 supply in the critical wall areas of the arterial vessels deteriorates when local wall thickenings (adherence of platelets) occur and, simultaneously, the resting $P_{O_2\text{-art}}$ drops, e.g. with increasing age. *In order to keep the development of arteriosclerosis in the vascular system at a low level, persons over 50 should – as explained in Paragraphs 3.4.4 and 5.2.2 – do everything in their power to raise their $P_{O_2\text{-art}}$, at rest, to as high a level as possible and for as long as possible.* As soon as a selected variant of the O_2MT has caused the narrowest capillary cross-section to be dilated (see Paragraph 1.1.1 and Figs **1** and **2**), the peripheral resistance in the circulation and hence also the blood pressure drop immediately and lastingly (cf. Paragraph 5.2.4).

Effects on the arterial side of the blood vessel system similar to those attainable by O_2MT can be gained by the clinical implementation of a *21-day fast* [350]. Details of the program of a juice fasting period in accordance with Krauss are compiled in Table **42**. How strongly the therapeutic effect of fasting influences the arterialization system of the lung, for example, can be seen from this finding: *in an experiment with 12 patients whose $P_{O_2\text{-art}}$ under conditions of rest was on average 72 mmHg, this resting value rose to 94 mmHg after physical-dietetic measures spread over 5 weeks.* The main contribution to this increase was made by the 21-day juice fasting period as in Table **42**. Like the effect of the O_2MT, the effect of fasting is multifactorial. One factor in fasting is the *improvement in the Broca index*, especially in overweight persons. A typical example of the improvement in this index possible by fasting can be taken from Fig. **265**. In other words, after the fast there is a *considerable saving* in circulatory work, which is expressed in a slight drop in pulse frequency. A further important effect of fasting is the *breakdown of waste products, e.g. from degenerated regions of the arterialization system of the lung and from the walls of the (arterial and capillary) vascular system.* The latter effects of fasting are discussed in [369]. It is reported that the protein deposits on the capillary walls, which lead to an increase in wall whickness from approximately 0.8 µm up to 2.3 µm (only) in diabetes mellitus, disappeared after fasting. It is known that the organism, in its lack of substrates, mainly falls back on tissue components that are inessential for life, superfluous or even harmful. If we bear in mind the results of observations of the eye-ground before and after fasting, and also of the strong lipolysis that occurs during fasting and which is even intensified by a low level of physical activity [350], this justifies the expectation that *fasting can also contribute to the breakdown of intra- and extracellular lipid*

Table 42 Program of the 21 day juice fasting period – clinical implementation [350]

1.	Methodology of the therapeutic fast
1.1	Serving the juice in 3 meals morning fruit juice midday vegetable juice or vegetable broth evening fruit juice
1.2	When juices with low vitamin C content (apple, bilberry or grape juice) are given as main juices, the daily ration of vitamin C must be ensured by a small quantity of additional, vitamin C-rich juice (e.g. 150 ml citrus juice, 40 ml sea buckthorn juice)
1.3	In case of thirst, reduction of the concentration capacity of the kidney, increased NPN in the blood, or during a fasting crisis, the fluid intake can be increased by tea
2.	Measures in the therapeutic fast
2.1	To ensure the patient's compliance he must be informed of the purpose, chances of success and the course of the treatment. Attention drawn to the fact that sensations of hunger do not usually occur and that possibly occurring critical moods are harmless
2.2	Bowel movement on the 1st and 3rd days by means of a (preferably saline) laxative. Intestinal enema (1/4 l) at body temperature daily if at all possible but at least at intervals of 2 days
2.3	Care of heat regulation. Warm clothing, covers, partial baths at increasing temperature
2.4	Dermal and mucodermal care. Mouthwashes and brushing the tongue several times a day. Small hydrotherapeutic measures, such as skin-brushing, washes, showers, compresses
2.5.	The faster's frequently felt need for peace and quiet must be taken account of in the surroundings.
2.6	Bland and light transitional diet at the end of the fast to start up enzyme secretion and peristalsis again. Under no circumstances a sudden transition to a normal diet. Diet sheet somewhat as follows: 1st day morning one grated apple midday one plate potato or cereal soup evening two pieces of fruit (ripe) one slice crispbread with a scrape of butter (5 g) 2nd day early 100 g "Kollath breakfast" 1 piece ripe fruit midday 100 g salad, or low fibre vegetables, 150 g potatoes evening fruit, 2 slices crispbread, 15 g butter
2.7	Fasting crisis with disruption of the vegetative system (e.g., depression, headache, vascular lability or flaring-up of symptoms of illness) to be cared for by additional administering of black tea, also coffee and 20 g honey
2.8	A light sedative and antispasmodic local applications of warmth are usually enough to revive the patient's sense of well-being

deposits in the wall of arteriosclerotically altered vessels (cf. Fig. 244).

The *equidirectional effects of the O_2MT and fasting* make it obvious to combine these two mutually complementary therapies in order to gain even stronger effects, especially on the arterial side of the vascular system. For this reason a period of juice-fasting was named as a further step in combination with the 36 h O_2MT variant GK 4-I. This must be clinically implemented, despite the extra cost and time involved.

Nature has adapted the vascular system to the high cardiopulmonal performance of youth and middle age. When increasing age leads to a drop in performance of the cardiopulmonal system and hence in the O_2 uptake, at rest, this adaptation deteriorates and arteriosclerotic damage looms. This damage is by no means evenly distributed over the whole of the arterial side, but is known to manifest itself with greatly increased probability at certain sites of the arterial network, e.g. at ramifications and endothelial lesions. Which area and which organ connected to it are first affected in the individual case depends on the chance nature of the vessel wall architecture (Fig. 264, vasa vasorum).

The localization of the pathological alteration in the arterial wall is largely decisive for the optimal design of the 3rd step of the O_2MT

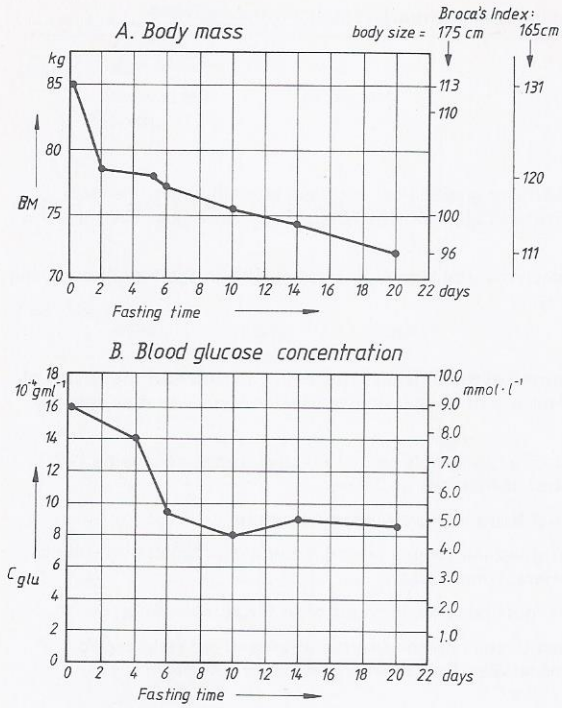


Fig. **265** Reduction in body mass or of the Broca's Index (A) and the fasting blood glucose concentration in a diabetic during a 21-day fasting period [350]

variant applied. The localization determines in each case the measures to increase circulation during the application of therapy (see Paragraph 2.3.5).

Arteriosclerotic or capillary vascular damage is often such that (first) the *blood supply of the extremities is impaired* [423]. In 70% of cases of this type coronary sclerosis occurs simultaneously [424]. Usually the peripheral arteriosclerosis or capillary constriction even precedes the coronary sclerosis. The first signs of weak circulation in the extremities (e.g. the onset of intermittent claudication) should always be taken very seriously and seen as ground for early therapeutic measures. We must never wait until there are signs that severe irreversible tissue damage (e.g. pregangrenous conditions), caused by O_2 or supply deficiency, have been triggered. That the permanent restoration of the O_2 status and of the COP, which declines with age, can lead to a decisive improvement of the situation is shown by the following case: in an older patient with so-called "smoker's leg" the pregangrenous situation was so advanced that the doctor ordered amputation within 14 days. The patient used this time for the implementation of the 36 h O_2MT procedure GK 4-I (cf. Table 27). He then presented himself for amputation in the clinic but the same doctor declared after examining the leg that amputation was no longer necessary. Amputation could also be avoided in several similar cases of this type. This is a particularly fruitful area of indications of the O_2MT.

In accordance with Chapter 4 the variants GK 2-I, GK 4-III and GK 7 with their measures in the 3rd step for the *improvement of the flow properties of the blood* by means of hemodilution [47, 114] are indicated for circulatory disorders in the extremities or certain organs. We would emphatically refer the reader here to the hemorheological papers [425, 426], the infusion of *buflomedil* (Bufedil), and the oral administration of *pentoxifyllin* [427].

In experiments of this type measurements of the mean tissue P_{O_2} (and the tissue temperature) behind the arterial or capillary constriction enabled us to pursue the O_2 situation before, during and after the therapy procedure, and hence gain *numerical data for the success of therapy* in the individual case.

A 51-year-old patient could be spared a bypass operation on the heart by means of the O_2MT variant GK 4-III (plus 4 HOT* treatments). Because of a poor exercise ECG, coronary angiography had been performed. It revealed a severe affection of the three coronary arteries. In the course of treatment η was raised from the critically low level of 13% to a lasting level of 31%. The cardiac complaints which had previously occurred even in minimal exertion did not take place. It is also possible to alleviate arteriosclerotic constrictions by the combination of O_2MT with EDTA (ethylene diamine tetraacetic acid) treatment; dose 3 g in a 50 ml infusion solution, supplemented by magnesium, vitamin B_6 and others; 20 treatments of 3–4 h twice a weak (decomposition of deposits in the arterial walls).

Finally, we would remind the reader of the noninvasive method of transcutaneously measuring the P_{O_2} in extremities after compression and lifting the blood flow combined with routine blood pressure measurement, described in Paragraph 3.4.4. These data enable us to define a relative parameter for the quality of a certain vessel (or vascular network) and its alteration due to stressful therapeutic influences. In connection with this we should refer to the pilot study into the reduction of the biological age by means of 15 years of O_2MT (see Paragraph 1.1.6).

5.3.10 Stroma, rheumatism, skin

The new formation of *stroma*, an energy-requiring process, occurs in the living organism wherever larger cell aggregates have decayed. Since this can occur anywhere in the organism and since the local tasks and potential of this reaction are consequently very varied (healing of all types of wounds, broken bones, tissue necroses etc.), the great variety of processes which transform biological material into stroma is easy to understand. One pathological process of this type, the unspecific mesenchyme reaction in the walls of the arterial vessels, triggered by sclerogenous noxae, has already been the subject of several parts of this book.

We will briefly describe one example from the treatment of cancer, as it illustrates the effect of this reaction from a completely different viewpoint: after a first strong therapeutic attack (cancerostatics, ionizing radiation) on a carcinoma, the cancer cells near the capillaries, in particular, which are well supplied and therefore proliferate rapidly, are killed. Just 3 days later histology shows that a *strong mesenchyme reaction (infiltration) has occurred at the site of the destroyed cancer cells near the capillaries*. This mesenchyme prevents the further diffusion of substrates, and the cancer cells distant from the capillaries and not destroyed by the primary therapeutic attack become very resistant to further therapeutic attacks. It was on this process that we based our mesenchyme theory [428] of the formation of resistance in cancer therapy protocols with fractionation.

A chance clinical observation tought us that *wound healing can be promoted and very greatly accelerated* by the interaction of long-term variants of the O_2MT. In one patient trophic disorders after long illness had led to severe decubital ulcers which would not heal. During the course of a 20 h treatment cycle with O_2MT and artificial raising of the blood glucose concentration to four times the normal level, the pressure points closed after approximately 6 days.

This indicates the feasibility of promoting and accelerating wound healing, if necessary also in combination with the stimulation of the body's own defense system.

Good results in the combat of *polyarthritis* using the 36 h (18 day) O_2MT immunostimulation, GK 4-IV variant (with thymus dragees) have been repeatedly reported. We would also refer to the administration of *interferon* [392] as an additional step.

Via the capillary fluid spaces of the *joints* and *bones* the O_2MT should also be able to aid in these areas in some disease processes. We are thinking here particularly of the alleviation of inflammatory processes [429--432] and harmful metabolic deposits in the complex rheumatic process by means of the raising of the O_2 metabolism, especially the permanent raising of the product $\eta \cdot$COP (relative characteristic value) and the stabilization of the lysosomes. Indeed, the O_2MT has proven to be so effective in the framework of rheumatism therapy (natural inhibition of inflammation and mesenchyme reaction, no side-effects as in cortisone derivatives), that its introduction into the *combat of rheumatism* is progressing well.

We must also mention the observations of a significant improvement of knee joint arthrosis (Dolina, Karlovy Vary, CSFR) and of the normalization after O_2MT of considerably raised triglyceride or cholesterol levels which had existed for years, and of increased blood sedimentation rate, for which no cause could be found.

Klopsch has reported on the improvement of the O_2 status after *chiropractic treatment*.

In connection with this we would refer particularly to combinations with the new high-frequency method (CMT Selectotherm procedure), discussed in Paragraph 1.2.2, which enables a high dose of heat energy to be transmitted even to stroma lying deep below the body surface.

Many years before the discovery of the O_2MT procedure and its effect of permanently raising the O_2 uptake, the procedure was performed in 1971 with roughly the same schedule as today on a then 64-year-old male, and was continued until 1980 at intervals of approximately 1 year. The pretherapy $P_{O_2\text{-art}}$ in 1971 was, on average, 78 mmHg and was only slightly above the expected level for the age of 64. From the beginning of 1977–1980 levels of the $P_{O_2\text{-art}}$, at rest of between 95 and 105 mmHg were normally found. At the age of 64, the skin on the face (eyes) was already showing clear signs of age. It was striking that these signs of age hardly increased up to the age of 78 years, i.e. until the end of 1986 (latest observations). If this first individual finding is later statistically proven, this would mean that the *ageing of the skin* can be delayed by permanently raising the arterial, and reducing the venous P_{O_2} at rest.

We have recorded 7 cases in our Institute in which female O_2MT patients spontaneously reported better skin tension (turgor), reduced

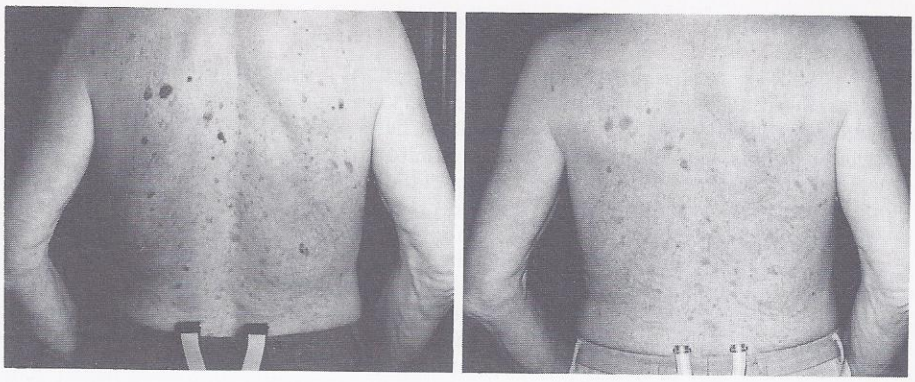


Fig. **266** Amelioration of possibly precancerous skin lesions in the back of a 73-yr-old male patient within 10 months through daily intake of a thymus dragee[1] and the securing of a permanently good O_2 status ($\eta \approx 40\%$; resting Q_{O_2} 0.34 l/min^{-1}) by 15 min O_2MT quick procedures. Daily brushing of the affected skin areas for 20 s. Left: 1.1.1984; right: 1.11.1984

[1] Thym-Uvocal® (Dr K. Mulli KG, D-7844 Neuenburg, FRG)

skin impurities (comedones) and improvement of acne.

Figure **266** shows an example of the effect of an O_2MT long-term variant, with the daily administration of one thymus dragee over 10 months, on the skin of a 73-year-old patient.

5.3.11 Defense. Multistep stimulation of the cellular defense

In the same way as the condition of the vascular system, the condition of the defense system is also of decisive influence on the individual's health status. It is known that the organism has a series of mechanism to defend itself from harmful living or dead matter:

1. *Unspecific mechanisms* by co-operation of certain types of cells, the *unspecific cellular defense* and, mediated by soluble factors, the *unspecific humoral defense*.
2. *Specific mechanisms* through highly specific chemical reactions, the immune reactions. Here the organism forms a quite specific defense substance, the *antibody*, against a defined noxa, the *antigen*. Its damaging properties are neutralized by binding the antigen to the specific antibody and its ensuing breakdown (antigen-antibody reaction). The immune globulins represent the fraction of antibodies within the blood serum proteins (specific humoral defense). T-lymphocytes together with other defense cells mediate the specific cellular defense.

All these defense mechanisms need energy, and consequently oxygen.

The main weapons of the *unspecific cellular defense*, the great contribution of which to the defense process has recently been clearly seen, are the polymorphnuclear cells, and the carriers of the specific cellular defense, the T-lymphocytes. One way of increasing the host's defense is to raise the number of these cells in the blood. One way of doing this is discussed further below (see Paragraph 5.3.13.4). Another way is to increase the impact of the defense cells in general or their functional elements on the respective target, in particular by means of energy-raising O_2MT procedures.

With our subject matter it is obvious that we should ask about the *changes in the host's defense system with advancing age*. The critical decline in the provision of effector substances with advancing age should be mentioned here. An example is the drop in thymus products in the plasma as a result of the advancing involution of this gland (cf. Fig. **239**). We have found no indication of significant changes in the number of defense cells with age. By contrast, it is reported in [433] that certain *autoantibodies* continuously increase from the age of about 70. Increasingly autoaggressive im-

ing values of the right-hand ordinate reflect the *augmented defense potency*, when the O_2 status and the variants of the O_2MT are appropriately considered. From the numbers of the left-hand scale the guiding principle can be drawn that *tumors should be immunologically attacked in their earliest stages of development*, if possible. The resulting advantage in the conquest of cancer also equals some powers of ten. The numbers of both scales reveal the necessity to adapt the anticancer strategy to the progress aimed for.

5.3.13 Application of the oxygen multistep immunostimulation in the various development stages of tumors and in various phases of treatment

Figure **268** shows a comprehensive presentation of the *cellular development of cancer*. It shows the avalanche of cancer cells growing from a single cancer cell, dependent on the number of cell doublings. The following time scale represents the cell doubling time t_D. The mean value of t_D is known to lie between approximately 50 and 200 days for primary tumors and significantly shorter, e.g. between 10 and 50 days, for the metastases, which are normally better supplied. In later examples we always assume the smallest (least favorable) t_D values of the named areas.

It is assumed today that cancer cells, which become the start of avalanches of cancer cells, arise relatively often from normal cells due to carcinogenic influences. These avalanches are normally caught and eliminated in their earliest stage by the unspecific defense (defense barrier). The regulating principles prevailing in this *possible silent phase* have already been discussed in [376]. They were seen in the fact that the power of defense increases more quickly than the number of cancer cells.

The host's "recognition" of a malignant lesion is not necessarily a specific immunological process in the sense of a classic antigen-antibody reaction, but is frequently triggered by anomalies in the metabolism and/or membranes of the transformed cells [447]. The differences between numerous tumors as regards localization, timepoint of their appearance, growth rate, metastasizing propensity etc. are very probably conditioned by the host's variously effective control mechanisms. As long as this great variety remains unscrutable, the *stimulation of unspecific* (immunological as well as non-immunological) *defense processes* gains particular significance from the practical point of view.

In accordance with the *guiding principle* of *implementing the immunological combat of cancer in stages with the smallest possible number of cancer cells*, the general cancer prophylaxis with O_2MT immunostimulation repeated approximately once a year should be given top priority among the combative measures. Even in fast-growing types of tumors it is rare for more than 10^3 cancer cells to grow from one cell in the course of one year. The timepoint for the prophylactic procedure would therefore lie at point A in Fig. **268**.

Without the counter-measure of significant stimulation of the defense, the avalanche would continue to develop to ever-increasing cell numbers. Under favorable local environmental conditions the cell avalanche overcomes the host's defense barrier and *cancer becomes manifest*. The uncontrolled tumor growth of the preclinical phase begins. According to these concepts, the *manifestation of cancer* is probably not so much conditioned by the occurrence of cancer cells from normal cells transformed by carcinogens, as by the level (fluctuating in terms of time and location) of the defense barrier (transition from phase I to phase II). The level of the defense barrier also undoubtedly has a decisive influence on the manifestation of recurrencies and metastases. The further development of the avalanche is facilitated when the level of the defense barrier is temporarily reduced, due to immunosuppressive influences for example. In connection with this it should be remembered that cancer occurs with increased frequency some years after organ transplants with immunosuppression, and also in the final stage of AIDS, which destroys the defense system.

After the *recognition phase* (early recognition), which lies between approximately 23 and 30 cell doublings, the actual disease phase (primary tumor) begins; this leads to death within one or more years, according to the mean t_D rate; if the primary tumor is not removed in time, then death occurs by point B in Fig. **268** at the latest. Even with wide excision, i.e. an operation that encompasses a sufficient margin of normal tissue, it is usually only possible to reduce the number of remaining cancer cells to approximately 10^9 (point C in Fig. **268**). This can then be further reduced to approximately 10^6 by means of chemotherapy and radiation therapy [448]. In many cases the natural level

of the host's defense is not sufficient to destroy 10^6 cancer cells, and tumors recur (point D in Fig. **268**).

During the classical therapeutic measures mentioned there is generally a dissemination of cancer cells. This triggers metastasis in about 50% of cases, leading to numbers of cancer cells between 10^5 and 10^6 [449] within 4–8 weeks after treatment of the primary tumor.

The *O_2MT immunostimulation*, applied at point A of Fig. **268**, would serve to realize a general cancer prophylaxis; applied shortly before point B, it can reduce the risks in surgical tumor removal; applied between points C and D, it can increase the quality of life and effectiveness of chemotherapy and radiation therapy, and, finally, applied at point D, it can provide a prophylaxis against metastases and recurrences. The details of these applications are discussed in the following paragraphs.

5.3.13.1 General cancer prophylaxis in the developmental stage with only 1000 cancer cells

It has already been pointed out that, in order to establish a *general cancer prophylaxis*, it is necessary to simplify as much as possible the procedure for the certain destruction of aggregates with approximately 1000 cancer cells, which is repeated annually. The effort required for a procedure like this should not be greater than the annual mass miniature radiography, which is usual today. The task of simplification also applies to O_2MT immunostimulation. The synergistic effects of this two-pronged procedure are portrayed in Table **43**. As shown in Paragraph 4.2.4, Fig. **227**, a significant simplification of the first factor, the chemical stimulation of the cellular defense, was attained by the administration of thymus dragees or Neythymun drops. For the second factor, the lasting improvement of the O_2 status, many years of research will probably be necessary to determine whether the 15 min O_2MT immunostimulation, GK 2-II variant, or even just the improvement of the O_2 status by means of drugs (cf. Fig. **235**) in combination with thymus dragees or Neythymun drops are of clearly detectable efficacy in the prevention of cancer.

Our discovery of the great significance of the O_2 status for the host's unspecific cancer defense is quite new and therefore not yet generally recognized. Figure **269** therefore shows an experimental finding that clearly shows the *influence of changes in the O_2 status on the strength of the host's cancer defense*. A basiloma of approximately 25 mm^3 was observed in a patient having an initially good O_2 status (η = 52%). Then he had influenza, which caused his O_2 status to deteriorate severely to η = 14%. As a result of the concomitant reduction in defense, the basiloma grew to 140 mm^3. After the influenza the good O_2 status re-

Table **43** Synergetic effects of O_2 multistep immunostimulation

Step	Phenomenon	Effect	Literature
1. Chemical stimulation of cellular defense by means of BA1 effect or thymus extract	Temporary increase in number of leucocytes + lymphocytes	1. Significant increase in number of defense cells for several days to weeks	von Ardenne-Reitnauer (1975 until 1980)
2. Energetic activation of cellular defense by increasing O_2 transportation to the whole body tissue with variants of O_2 multistep therapy	Temporary increase of O_2 transportation to up to 250% of the average rate for a 70-year-old, for some days. Triple synergistic effect. 2.1/2.2/2.3 Increased phagocyte activity	2.1 Stimulation of cell motility through improved energetic situation[1]	von Ardenne (1979 until 1980)
		2.2 Stimulation of chemotactic attraction	Richter (1980)
		2.3 Stimulation of formation of peroxides in the phagocytic cells[1]	Fischer-Staudinger (1980) (role of peroxides as principal weapon at phagocytosis)

[1] Energy/O_2 consuming processes. An idea of the strong influence of the O_2 status alone on the potency of the cellular defence, can be gained from the in vivo observation of a basiloma in Fig. **269**

passed. There are several reasons for this: latent period of metastases, recognition of a cure only possible after a minimum of 5 years, lack of research capacity in the responsible clinics etc. In the meantime an alarming number of cancer patients die of their disease every day.

A further severe obstacle to the accomplishment of progress in the health service arises from the *flooding of doctors with literature and information*. No less important a doctor than R. Gross stated a few years ago that more than 95% of specific medical literature is thrown unread into the wastepaper basket. This leads to the hard but realistic conclusion that, under the conditions of our time, the publication of results in medical journals is no longer enough, as was the case 50 years ago, to achieve a fast transition into practice. The firm conviction that the O_2MI and the O_2MT are of great importance for many branches of medicine *obliges* the author to ensure its fast transition into practice using non-standard methods which are, however, adapted to the conditions of our time. The following procedure results from this:

1. Scientific publication of results in journals, books and by lectures at specialist symposia or congresses (only slightly effective).
2. *Information to directly interested patients or laymen* via all types of mass media, i.e. television, radio, the press, magazines etc. (extremely effective). The patients then force their doctors to deal with the subject in question.
3. Production of several thousand copies of every paper with what appear to be important contents. Copies sent on request (from our Institute) to patients, perhaps to be passed on to the doctors treating them.
4. Printing and sending (on request) of a *list of doctors, clinics and institutions* solidly implementing the treatments in accordance with the schedules elaborated.

5.4 Closing remarks

Looking back, we must note the *extraordinarily high number of indications for O_2MT*. Very recent individual findings point to further, probably relevant indications such as the alleviation of states of confusion and the side-effects of many drugs, increase in IQ, application during births, reduced risk in operations, acceleration of wound healing and rehabilitation, and the combat of multiple sclerosis (inhibition of attacks). For physically disabled (e.g. paralysed or amputated) persons who are subject to the long-term stress of physical inactivity, the periodic repetition of variants of the O_2MT adapted to their specific situation can be life maintaining. The large number of indications is an expression of the unique universality of the O_2MT and of the fact that O_2 deficiency (energy deficit) is the primary cause of so many illnesses and complaints.

Only clinical practice can show where, in pathogenetic chains with many members, the therapist must set other priorities than the direct combat of oxygen deficiency. Several changes, supplements and refinements of the present-day methodology will certainly be developed from practice.

It is also very striking that there are *few absolute contraindications* for this therapy, as long as the P_{O_2} increase of the inhalation air in the 2nd step is not raised above the prescribed limit and, in the 3rd step, the possibly intended physical exertion takes account of the individual's capacity. In particular, there have not so far been any additional disorders in the regulative behavior of patients with regulatory disorders when the therapy is timed in accordance with Tables **24–33**.

The research into physiology, technology and the medical application of the O_2MT, compiled in this book, resulted alongside – or, rather, from – our efforts, begun in 1963, to develop the *Cancer Multistep Therapy* (CMT). This development, which will continue to occupy us in Dresden, led in 1977 to the design of a highly selective cancer therapy, with irreversible inhibition of the blood microcirculation in the cancer tissue. Its direct target is now, after positive animal experiments and pilot studies (e.g. Fig. **82**) to furnish further clinical evidence of the high therapeutic selectivity attained. Here, too, the stimulation of the metabolism of the cells and the influencing of the microcirculation form the methodological key. Here we were mainly concerned with the stimulation of the glucose metabolism, i.e. the long-term multiplication of the aerobic glycolysis of the cancer cells, which is possible in the deficiently supplied cancer tissue and leads to its strong, selective over-acidification with many therapeutically utilizable effects. Thus a

multitude of stimuli to the content of this book must be put down to our work on the cancer problem. It can be clearly seen from the facts of repeated considerable aids to the elaboration of the CMT concept arising from results of O_2MT research, and from the application of the O_2MI in the various stages of development and combat of cancer, that it was very productive to describe simultaneously the apparently very different paths of the CMT and the O_2MT.

The discovery and utilization of the capillary switching process of the blood microcirculation, which forms the basis of the O_2MT, has made it possible to *increase, long term, the energy in the human organism by approximately 15% (in healthy persons) to 80% (in weakened persons)*. This fact, which has far-reaching consequences for medicine and the health service, was proved and evidentially documented in 1986 by spirometric measurements of the lasting rise in CO_2 production at rest.

The energy largely to re-write this book in the course of 2 months stems from two sources: from my purposeful utilization of the O_2MT procedure, and from the response to the objections and criticism made by fellow specialists such as contained in the letter from Otto Warburg, printed below, which is one of the most moving letters calling for action that have ever reached the author.

Perhaps the text of this letter written on the occasion of the 1st edition of our Cancer Multistep Therapy book [2] can also support many a reader in his personal fight for the progress of science.

Max Planck Institute
of Cell Physiology

Berlin 33 Dahlem
Garystr. 32

1. 4. 67

Dear Prof. von Ardenne,

I must say that I admire you when I leaf through the book. In these few years you have certainly reached the peak of cancer research; I certainly know of no single book in the whole of cancer research in which anyone else has tackled the therapy problem with the same energy and breadth. My instinct tells me that, in the long run, your victory is certain. You can only make *one* mistake now: in giving up too soon, discouraged by too much opposition. Perhaps I could be exemplary in this respect. The more opposition I found, the more I attacked and the better my weapons became.

"To dust with all enemies of Brandenburg!"

Yours sincerely

Otto Warburg

Supplement

Since the publication of the 4th German edition (1987) new results have been gained, which are detailed in the following three original papers Nos. 373, 374, 375 and 380 of our publication list.

It has been found that there are two basic types of action of oxygen multistep therapy. In specific studies using mostly large numbers of individuals, the efficacy of the oxygen multistep therapy and oxygen multistep immunostimulation has been demonstrated by the improvement of about 30 physiological parameters (primary and secondary effects). There are only few therapeutic regimens in the history of medicine, the positive effects of which could or can be proven by measuring of numerous parameters. In the long run, scientific truth has prevailed over methodological errors and prejudice.

The consideration of the human body in terms of physical energy and its dynamics may be strange in established medicine, but is nevertheless obvious. Since 1987 the author has passed more and more on to considering general issues of the human body and life, as well as the problems of illness, immune defense, therapeutic effects, health and age, from an energetic point of view.

New findings have resulted in supplementing the definition of the *oxygen status* (arterial oxygen partial pressure $P_{O_2\text{-art}}$, at rest; venous oxygen partial pressure $P_{O_2\text{-ven}}$, at rest; value of η; O_2 uptake at rest; maximum O_2 uptake) by ergometric measurements of the *energetic status* (charge maximum during 2 min, PWC test). Several more detailed explanations of the energetic status of man, the deterioration of this status with progressing age, the energy consumption by illness and stress, as well as of the improvement of the energetic state and, hence, the energetic reserves by means of physical exercise and oxygen multistep therapy are given.

Studies of the proportionality between the energetic state and the cancer cell-killing capacity of the defense mechanisms of the body have made it reasonable to report in more detail on the different concepts of combatting cancer by using the oxygen multistep immunostimulation. Many clinical results obtained by our medical partners and ourselves indicate that these concepts will become an indispensable element of future anticancer strategies.

Note that each part of the supplement has its own reference list.

Dresden
Weisser Hirsch, July 1988 Manfred von Ardenne

Detection of the persistent elevation of oxygen uptake, at rest, carbon dioxide production, respiratory minute volume and performance reserves after oxygen multistep therapy[1]

Introduction

Oxygen has been used in medicine for more than 100 years. The oxygen multistep therapy (O_2MT), however, differs basically from all other kinds of oxygen application now known to medicine by the following discoveries:

I. The discovery of the *switching mechanism of blood microcirculation*, which is effective in the whole blood and is controlled (or controllable) by the oxygen partial pressure at the venous end of the capillaries ($P_{O_{2\text{-ven}}}$) [1, 2, 3]. Once triggered, this mechanism can result in *lasting effects* – in a negative (under O_2 deficiency) or positive (under O_2 excess) direction.

II. The discovery that O_2MT procedures are capable of re-elevating the previously dropped blood microcirculation for weeks, months or even years [3, 6], provided that the oxygen flow is individually adjusted to the physical strain (3rd step of the treatment schedule) and to the respiratory minute volume (RMV; 2nd step) over the prescribed timespan of treatment (15 min at high exertion; 36 h at very low exertion). The outcome of this "high-charging" is two easily detectable effects: the persistent elevation of the uptake of oxygen, measured *at rest*, and of *maximum* O_2 uptake, which is related to the physical working capacity [3, 6] – in other words: there is a *lasting increase in the power reserves of the body*.

III. The discovery that distress, according to the classical definition coined by Hans Selye, and in a more comprehensive sense (physical inactivity, infections, toxins, such as from cancer chemo- and radiotherapy), severely worsens the *resting O_2 status* [3].

IV. The discovery of *relations between the efficacy of the host's defense*, mainly its cellular anticancer defense, and the *quality of the oxygen state*, at rest. This discovery is utilized to increase the effects of conventional cancer therapies, preferably to reduce their side-effects, and the rate of metastasis, as well as to give support by high-degree stimulation of the host's anticancer defense [3].

Despite numerous publications (2 books, 94 papers and lectures) our measurements, and hence the efficacy of O_2MT, have repeatedly been doubted. Particularly, there are cetain critical comments in that the patients could not make use of the excess oxygen provided in the breathing gas administered.

Therefore, this study was undertaken in order to test whether or not changes of the respiration or oxidative metabolism occur due to O_2MT.

Materials and methods

The breathing gas measuring and analyzing system Oxycon-4, manufactured by Hellige, D-7800 Freiburg, FRG, was used. This device simultaneously determines respiratory minute volume (RMV) and rate, tidal volume, expiratory differences of oxygen and carbon dioxide, respiratory quotient (RQ), oxygen pulse, respiratory equivalent, and metabolic units (MU)[2], and delivers a printed protocol. The gas volumes are automatically corrected for BTPS and STPD conditions.

In the first series, the parameters mentioned were measured at those individuals who had received either the standard treatment (36 h procedure) or two times the quick procedure (QP); in few cases, the latter was given in the 5 x 20 min variant [3].

The measurements were made before and 1–3 days (weekends in between) after termination of the respective treatment, as well as 2–4 weeks thereafter in order to detect long-term effects (10 patients living outside did not comply with this follow-up check). In a preliminary test we looked how far our measuring conditions deviated from the RQ standard procedure. For the relaxed, sitting subject we found that O_2 uptake and CO_2 release were higher by about 30% as compared to the stand-

[1] Published separately as our paper No. 373

[2] 1 MU = 3.5 ml O_2 per kg body weight and min; it represents the basic oxygen consumption of a sitting individual, at rest

The mean initial values of the group II individuals, however, reached the upper limits of normal; the people frequently showed signs of central nervous or cardiopulmonal hyperfunction. As to age and RQ, there were no differences between both groups before O_2MT treatment.

It is known from results of basic research that animal tissues reduce oxygen requirement and turnover, when O_2 supply and tissue P_{O_2} deteriorate, in order to escape an absolute oxygen deficit with its disastrous consequences [5]. So an equilibrium between O_2 supply and demand at a subphysiological level is established. A state like this is obviously present in senile hypoxidosis and in our group I patients as well.

Similar conditions are probably also responsible for the "spirographic oxygen deficit" according to Knipping, the interpretation of which by pneumology has been difficult to now. Due to the significance of this phenomenon, Knipping is quoted literally [11, p. 197] "Leaving out the mere filling deficit, the spirographic oxygen deficit represents an additional uptake of oxygen for covering a chemical oxygen debt or a true metabolic change from hypoxybiosis to normoxybiosis. The spirographic deficit is divided into

a) small, short-time, arterial and
b) longer lasting (up to saturation) deviations which are due to the increased oxygen tension in the tissue (up to 300 cc), as well as
c) long-term changes of metabolic nature ..."

This spirographic O_2 deficit, i.e. an increased uptake of oxygen after switching over from air to oxygen breathing, can be observed at rest and on exertion as well. It may occur as "hidden or compensated deficit" (Knipping) also in healthy subjects. Gerasimov [9] speaks in favor of the possibility of storage of "unnecessary oxygen" (NAD, NADP, pyruvate, mixed disulfides).

As known from the literature, there are frequently latent, not detected, hypothyreoses in the elderly. The patient sample of group I, having lowered O_2 uptake at rest, may include such subclinical cases. Special thyroid function tests, however, were not performed.

After another form of oxygen therapy, the hyperbaric O_2 treatment, a renormalization of the thyroid hormone levels was found (elevated values dropped and *vice versa*). This effect, accompanied by an improvement of the general state, persisted for 4–6 weeks [15].

During our follow-ups (repeated measurements on the following days without treatment), there were no significant deviations detectable. The highly significant increases of O_2 uptake, CO_2 production and RMV by about 19–25% must consequently be a result of O_2MT. Measurements made 2–4 weeks after termination of treatment provide evidence that these effects belong to the long-term changes of metabolic nature in Knipping's category c) (see above). In some patients (Nos 28, 29, 33 and 37 of group I) there was an effect on the O_2 uptake not before this time-span.

The higher increase in CO_2 production (+ 25%) as compared to that in O_2 uptake (+ 18.8%), detectable shortly after treatment and 2–4 weeks later as well, requires a particular comment, because this difference is responsible for the increase in RQ from 0.80 to 0.84. Even if a certain hyperventilation of some individuals is to be assumed during the measurement after O_2MT (e.g. Nos 11 and 13 of group I, who additionally made breathing exercises during O_2MT), the named differences remain significant after deduction of these two "deviators". There are obviously other reasons for this phenomenon.

Rapoport [13] described other biochemical sources for CO_2 in addition to the main pathway, the citric acid cycle. Significant reductions – partially occurring after preceding overshooting – of serum uric acid, creatinine, cholesterol and triglycerides demonstrate that O_2MT interacts with fat and protein metabolism in a not yet fully elucidated manner [1, 8].

It is known that RQ drops during oxygen breathing (hyperoxia) [16]. This effect is explained as a shift of the energetic metabolism towards a stimulated utilization of fatty acids. Moreover, it is of importance that the O_2 and CO_2 stores, the amount of which can only be assessed, cannot serve to explain the extent of these changes. They must be a matter of true metabolic modifications (Pasteur effect: inhibition of glucose oxidation and of formation of lactic acid by glycolysis).

From which sources of the intricate metabolic pathways the excess CO_2 arises after the return to normal air breathing, certainly needs further investigation.

Due to the known feature of CO_2 to act as the most important respiratory stimulant, the increase of RMV by 23% (still 18% after 2–4 weeks) can be attributed to the elevated CO_2 production.

Group II: In this group, the subjects of which exhibited higher values of O_2 uptake, CO_2

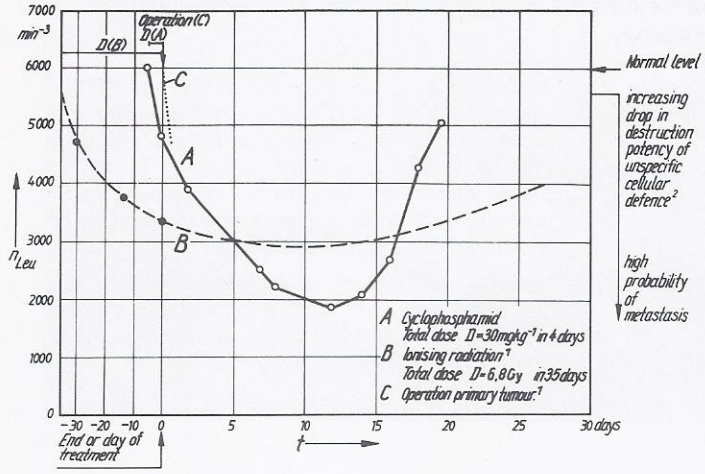


Fig. **293** Measurement examples of the drop in the number of leukocytes n_{Leu} (leucopenia) after a single impact of cytostatics (A), ionising radiation (B) and surgical treatment (C)

[1] Volume of primary tumor ≈ 800 cm³
[2] Reduced pH level in the cancer tissue increases chemotactic attraction

destroying them, because it is critically weakened in this of all phases, for reasons already discussed. Here, the reduced killing potential of the defense mechanisms might be in the order of $2 \cdot 10^4$ cells. These relationships, which can be taken from our research, led the author to the following, immediately applicable *variant with conventional cancer therapy and adjuvant oxygen multistep immunostimulation* [15].

In the first phase of therapy every effort is made to minimize the number of surviving cancer cells using established methods: surgical cytoreduction and (postoperative) irradiation, plus drug treatment, particularly in the case of already present metastases (Fig. **295**). The aim is to bring the number of cancer cells escaping the attacks down to $\leqslant 10^6$. Then, in accordance with Fig. **294** as adjuvant measure, the variant of the 36 h/18 day oxygen multistep immunostimulation, GK 4-IV, is applied; at first twice, simultaneously with the radiotherapy and (or) chemotherapy and, in the final repetition, to kill the remains of the still surviving malignant cells.

With this combined treatment the patient gains all the advantages and effects which present standards can offer in his case. The attending oncologist needs neither special training nor extra equipment, if he is willing to release the (still sufficiently fit) patient for 2 hours daily for outpatient treatment at a nearby oxygen multistep therapy center (see list of addresses) during the usual therapy phase.

The adjuvant procedure is never harmful. There is no medically reasonable argument against the utilization of this concept. The patient at least experiences the diminished side-effects of radiation and drug therapy and gains a higher quality of life in this phase of his disease. Moreover, as already mentioned, the stimulation of the host's antitumor defense means a considerable increase in the efficacy of established cancer therapies, which must lead to increasing cure rates and decreasing metastasis.

7. The cancer multistep therapy concept — still a matter of research

Despite the high standard attained in technique and equipment of the cancer multistep therapy [1, 15–17, 33–35], at present we do not inform the mass media about any progress achieved, because the few existing facilities are unable to provide comprehensive aid due to limited treatment capacity. Any public comment would rise unrealizable hopes now and in the near future.

The *cancer multistep therapy* (CMT) consists in the meaningful combination of the methodologically and technically sophisticated single steps of *hyperthermia, hyperglycemia and hyperoxia.*

The basic concept of 1965 already contained the selective main steps of all modern variants of the CMT:

A. The *hyperthermia step*, already in a two-stage form, by which the target (cancer

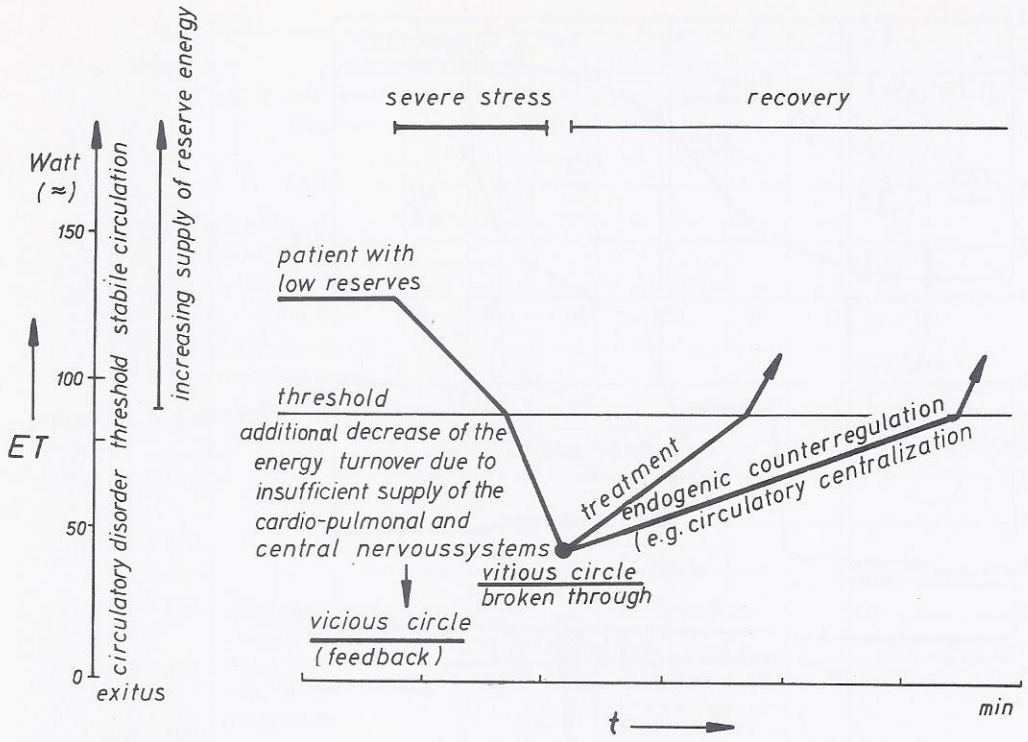


Fig. **303** Schematic course of a circulatory disorder, seen from an energetic point of view (the given values are approximative); ET = energy turnover

5. The permanent increase of the energetic reserves, lasting for many months, as the main effect of the oxygen multistep therapy

Oxygen has been used in medicine for more than 100 years. The oxygen multistep therapy (O_2MT) and its application basically differ from all other kinds of oxygen administration used to now in medicine by using the discovered switching mechanism of blood microcirculation, which is effective in the whole body [4–6]. Once triggered, this mechanism results in lasting effects – in a negative (under O_2 deficiency) or positive (O_2 excess) direction. O_2MT treatment effects the restoration of the diminished blood microcirculation for weeks, months or even years [7, 8]. The outcome of this "high-charging" is two easily measurable effects: the permanent increase in the O_2 uptake, measured at rest, and in maximum uptake, i.e. physical working capacity [9] – in other words: there is a lasting increase in the power reserves of the organism.

The compilation of results in the second part of this supplement demonstrates that the physical reserves can be augmented in weakened patients (group I) as well as in healthy volunteers (group II). The same paper gives information on the objective, individual recording of spirometric measurements and on some results obtained.

The increase in the physiological performance as the main effect of the treatment is usually measured on a bicycle ergometer by determining the exertion (expressed in watts) which is necessary to achieve a pulse frequency of 100, 110, 130 or 150 per min, respectively; it is the known PWC_f test which is done some days before and after the therapy. For further details see paper No. 374 (this appendix, p. 330).

The occurring long-term gain in physical energy reserves effects the improvement of numerous physiological parameters, which are conveniently measurable. The improvement of the energetic (or oxygen) status has been proven by measuring 9 primary effects (Fig. **304**). This improvement is further detectable from numerous

Status	Primary parameters determining therapeutic efficiency, healthy state and performance reserve	Achievable gains (approx.)		Remarks	
		Mean	Range	Our paper N	References
1 Energetic status	1.1 Maximum load capacity (measured in watts) (status quo ante)	age-dependent (see Fig. 2,17)		N° 373	[33]
	1.2.1 Gain in mechanical performance (measurement of PWC)	+17 to +29%	+3 to +94%	N° 297,373	[9], [33]
	1.2.2 Maximum aerobic endurance capacity (maximum aerobic lactate steady-state)	+9%	+4 to +25%	374, 378	[10], [35]
	1.2.3				
2 Oxygen status	2.1 Maximum oxygen uptake (spiro-ergometric measurement)	age-dependent (see Fig. 1)	+14 to +103%	N° 373, 374	[33] [10]
	2.2.1 Oxygen uptake at rest (spirometric measurement)	age-dependent (see Fig. 15)	-20 to +100%	N° 373, 374	[33] [10]
	2.2.2 CO_2-production at rest (spirometric measurement)		-23 to +100%	N° 374	[10]
	2.2.3 Arterial oxygen partial pressure $pO_{2\text{-art}}$ at rest	age-dependent age > 60	55 to 100 mmHg	N° 199	[4]
	2.2.4 Venous oxygen partial pressure $pO_{2\text{-ven}}$ at rest	age-dependent	55 to 20 mmHg	N° 267	[5]
	2.2.5 Arterio venous saturation difference η	age-dependent	10 to 60%	N° 289	[6]
	2.2.6				

Fig. 304 Parameters measured for the relative and absolute determination of the energy and oxygen status before and after oxygen multistep therapy treatment. Main effect: long-lasting increase of the mechanical performance reserve. Nine primary parameters

(secondary) physiological parameters. Nineteen of them are listed in Fig. **305**, including their improvements or changes. As an illustration, Fig. **306** shows results of short-term memory tests (secondary effect 1.1.) obtained on 59 volunteers, which revealed statistically significant improvements.

How long the positive primary or secondary effects of O_2MT treatments last will depend on whether the patient (proband) makes use of the increased physical fitness (energetic status) by passing over to a strenuous lifestyle. A regular physical exercise (sports in general, step-climbing, cycling, swimming, uphill walking, jogging etc.) for at least 10 min a day, where the pulse should rise up to f = 180 minus age according to Hollmann's rule is to be envisaged. Depending on age, sex and fitness, the necessary exertion should be in the range between 50 and 150 watts. The diagrams shown in Figs **307** and **308** for swimming and running are considered to ease the assessment of the respective load.

Our studies have been reported on in three books [1, 7, 11] and in numerous original papers. The elevation of the physical working capacity, long persisting after the termination of the oxygen application, can be considered a fact scientifically proven by the measurable effects on almost 30 physiological parameters [12–16].

Since energy is the prerequisite of all living processes, and hence energy deficiency, the primary cause of many disorders of vital functions, a therapy that attenuates or abolishes energy deficiency must be of great universality. This is the reason why the oxygen multistep therapy yields outstanding results in so many and so different therapeutic fields, e.g. combatting angina pectoris, arrhythmias, dyspnea, hypertension, hypotension, cerebral and peripheral circulatory disorders, liver diseases, impaired vision, side-effects of drugs and, particularly, cancer. For longer than 10 years the approval of this therapy was hampered in the Federal Republic of Germany, because the German Society for Pneumology and Tuberculosis gave more credit to its expert studies [17–20], which thereafter proved to be unsatisfactorily founded [10], than to the measurements of the author [21], who was already around 1930 by virtue of writing two books [22, 23] one of the pioneers of medical-electronic measuring methods and who, as a founder and president (1961–1974) of the Society of Biomedical Technology in the GDR,

Targets	Secondary parameters improved by long lasting increase of the energy status	Gain (approx)		Remarks	
		Mean	Range	Our paper N°	References
1 Brain CNS	1.1 Short-term memory parameters	+21%	19 to 23%	N° 379	[34]
	1.2 Critical flicker fusion				
	1.3 Velocity of nerve conduction	+ 10 %			
	1.4 Visual and acoustic reaction time	− 14% (≈60 years)	−3 to −40	N° 336	
2 Eye	2.1 Reduction of presbyopia (dioptric improvement)	Frequent observation			
	2.2 Reduction of glare sensivity Intra-ocular pressure	Frequent observation			
	2.3 Range of accomodation	Frequent increase			Also changes of the ocular fundus
3 Heart	3.1 ECG at rest and at exercise	Mostly normalization		N° 273	
	3.2 Arrhythmias	Mostly disappearance		N° 273	
4 Lung	4.1 Respiratory minute volume RMV	+ 23%	1 to +100 %	N° 373, 374	[33] [10]
	4.2 Vital capacity peak flow	+ 6.5 + 15 %			
5 Blood pressure	5.1 Blood pressure at rest (drug dosage reduction possible)	Improvement (normalization)		N° 129 (hypotension)	
	5.2 Blood pressure at exercise				
6 Micro-circulation	6.1 Blood flow measurement (e.g 133 Xe clearance)	+10 to +400% (extremities)			
	6.2 Walking range testing (standard, with metronome or running belt)	to 1000%			
	6.3 Quality of arterial vessel sections (RR-tcp O_2 test)		0.019 (45 years) 0.0096 (80 years)		
7 Accessory clinical findings	7.1 Detection of enzymopathias e.g. transaminases (liver)				
8 Biological age	8.1 Determination acc to Ries and Pöthig using the "Geromat" system		Decrease by 15 to 22 years (age range −75 yrs.)		
9 Cellular defense	9.1 Determination of the cancer cell killing potential on tumor patients before and after treatment with the O_3-MT procedure GK 4-IV		10^4 to 10^{11} cancer cells		
	9.2 Determination of the phagocytosis capacity of PMN's after stimulation with zymosan		400 to 1000%		
	9.3				

Fig. 305 Secondary parameters of different body sections showing improvement by permanent increase of the energetic status. Positive effects on almost all values. 20 secondary parameters

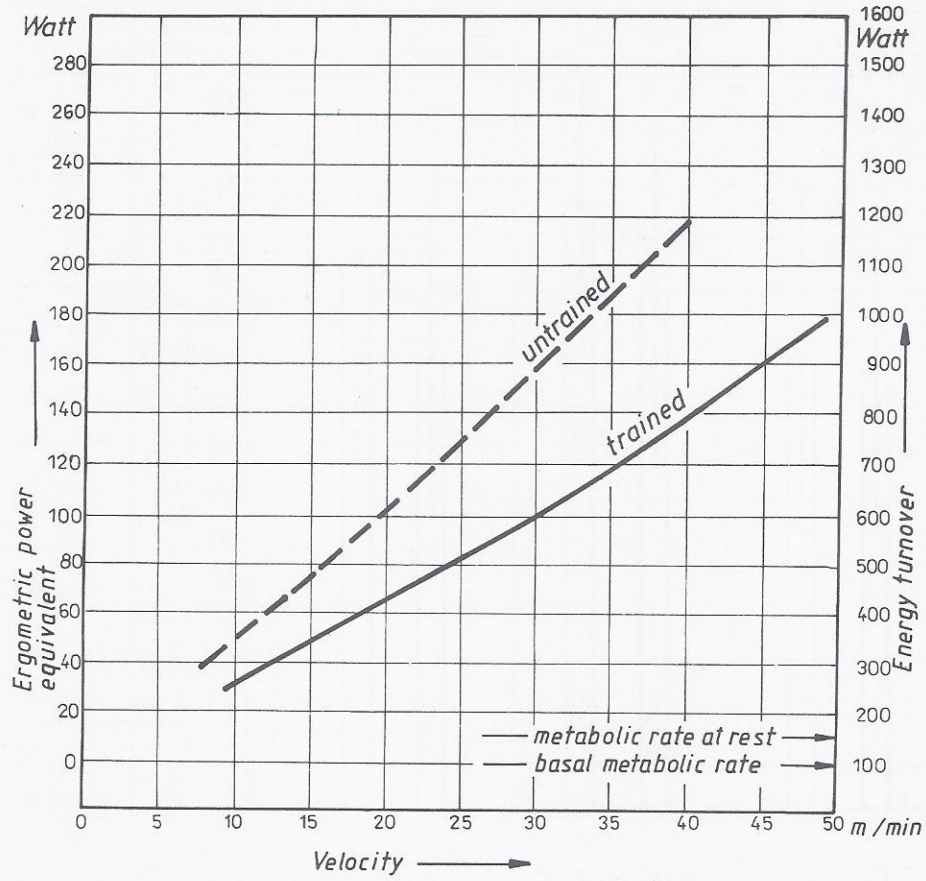
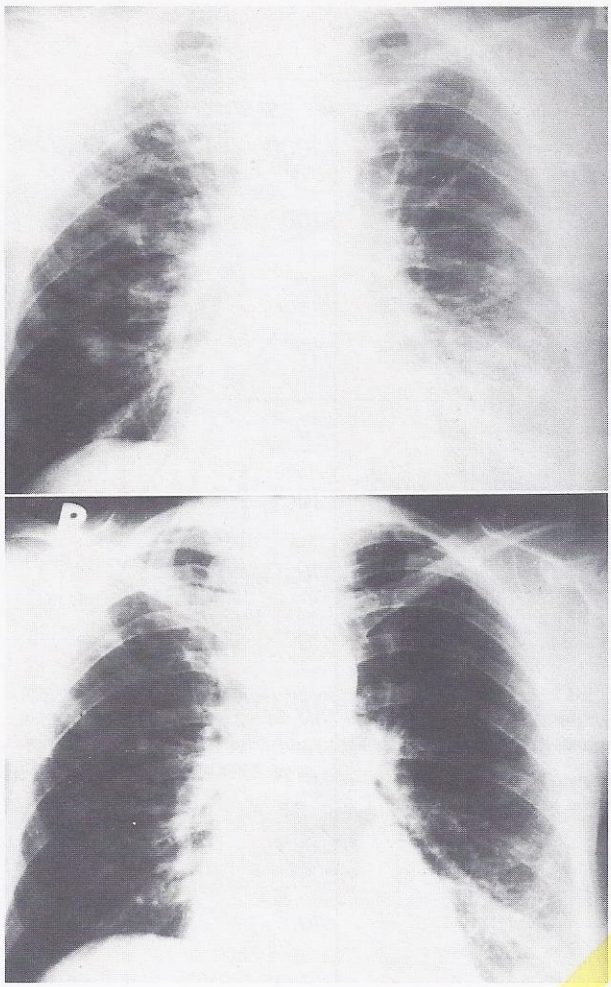


Fig. **307** Mechanical performance reserve MPR (ergometric power equivalent) and biochemical energy turnover in breaststroke of untrained and trained male persons (70 kg b.w.)

6. Very strong increase of the host's unspecific (anticancer) defense by long-lasting improvement of the energetic reserves

The commonplace observation that all processes of the host's defense consume energy led the author in 1971 to the concept [24, 25] and to the development [7, 26, 27] of a therapeutic variant called "oxygen multistep immunostimulation". In this procedure, the persisting elevation of the energetic status (by O_2MT) is combined for the first time with the effects of immunomodulators (biological response modifiers), which results in a surprisingly high increase of the capacity of the unspecific (anticancer) defense. This observation has gained specific significance for fighting tumors and metastases by another discovery [13], namely that the energetic reserves of the organism are severely reduced by distress, particularly by conventional chemo- and radiotherapy of cancer. The consequences drawn from these facts [7] and the relationship between the efficacy of the host's anticancer defense mechanisms and the energetic status of the organism [28] are now generally or individually utilized in order to reduce metastasis [29, 30], to give immediate aid during chemotherapy (in terms of quality of life, therapeutic efficiency, white blood picture etc.) and to reduce the probability of metastases during conventional anticancer therapy.

An experimental study mentioned in [11] revealed that the formation of immune cells is stimulated by increasing the energetic status (Fig. **309**).



a

b

Fig. **311** X-ray pictures demonstrating the partial remission of lung metastases after one treatment with oxygen multistep immunostimulation, variant GK 4-IV; attending physician: Dr Maruschka, Waren/Müritz, GDR. Patient: K. H., 49, mammary carcinoma, ablatio mammae; lung metastases since 1985; progressing growth despite drug therapy (terminated January 1987); bad general condition until August 1987
a State on June 16, 1987, before treatment: metastases in both lungs, multiple circular foci. Treatment: August 1987
b State on November 27, 1987, 12 weeks after termination of oxygen multistep immunostimulation treatment, variant GK 4-IV. Partial remission of lung metastases; improvement of general state

In another study (M. von Ardenne and H. Günther, unpublished results, 1988) the phagocytic activity of polymorphnuclear cells in human blood was studied by measuring their chemoluminescence after stimulation with zymosan. After treating healthy volunteers with the 15 min oxygen multistep quick procedure GK 2-I, the luminescence of the PMN cells was 5–10 fold higher as compared to the initial value before treatment.

The dimension of the progress made in terms of the number of cancer cells killed by the defense mechanisms can be taken from the scale in Fig. **310** [7] and amounts to 10000 cells. An illustration of this action is given in Fig. **311** for a case of lung metastases. About 10^{10} cancer cells were destroyed only by oxygen multistep immunostimulation (without drug or radiation therapy). An approximately comparable case (destruction of metastases from a melanoma) is given in [11, p 237]. In Fig. **312** another case is documented: female patient, 63, metastases of a melanoma in the upper arm, spontaneous fracture; rapid callus formation after treatment with oxygen multistep immunostimulation; exercises possible after 3 weeks; union after 6 weeks.

These and many other similar observations indicate a "killing capacity" of the oxygen multistep immunostimulation in the order of 10^9–10^{10} cells, i.e. masses of malignant tissue in the range between 1 and 10 g. When the tumor mass exceeds this upper limit, any success as to complete tumor eradication only by the process of oxygen multistep immuno-

7. Uninterrupted maintenance of the elevated energetic status by timely repetitions of the therapy

In order to minimize risks of health in older age, the good oxygen or energetic status once achieved by O_2MT is to be maintained as long-lastingly as possible. This recommendation is based on two reasons:

1. to minimize periods of insufficient supply to the middle areas of the vessel walls (contribution to minimize arteriosclerosis [7];
2. generally to minimize the dangerous time of a low (age-dependent, critically reduced) oxygen status.

How to realize this recommendation with the lowest possible expenditure of time and money?

Measurements concerning persistence or decline of the O_2MT effects are summarized in [1, 7]. The duration of effect depends on whether or not the treated person makes use of the additional energy produced in the body, as already discussed in Section 5. of this paper. If a strenuous lifestyle is adhered to, the effect lasts up to 1 year or above.

In a non-selected patient sample of a sanatorium the O_2MT effect dropped within approximately 7 months to 50% of the value measured immediately after termination of the treatment. In physically less active patients (unable to move, restricted mobility, indolence) a reduction of the same order occurred after about 3 months. For such a circle of patients treatment must be repeated after this period of time, if a drop below 50% of the therapeutic effect is not tolerated.

The necessity of ad hoc treatments is often caused by stressful events. Influenza and other infections, vaccinations, intoxications, surgical interventions, severe mental stress, long-lasting bedrest or other periods of unvoluntary inactivity belong to these events [7]. It is generally advised that the patient him(her)self endeavors to be O_2MT-treated again after events like these.

It is general experience that even in normal life stressful influences are so numerous that 1–2 annual treatments are justified. For individuals leading a nervous, restless and stressful life, the number of necessary repetitions can be markedly higher. At least in such cases the question of costs and time needed gains increasing interest. It must be assessed that these issues, which oppose a general application of the O_2MT to all social classes, can only be perpetually solved by treatments in the own home.

However, the patients must not think that this type of treatment goes without the doctor [1]. As a rule, the first treatment will be given in a specialized O_2MT center under supervision of an experienced physician. A check-up, the selection of the most favorable treatment variant for the individual case and the supervision of the first session (choice of exertion, ECG monitoring and others) belong to the undeniable medical duties. Another task of the doctor during the continuing treatment at home is the determination of the oxygen (i.e. energetic) status before and after treatment, i.e. the therapeutic success. The best form of cooperation between the "home-patient" and the attending doctor must be still found out in daily practice.

8. Selection of the individually adjusted variant of the oxygen multistep therapy

The different variants of O_2MT, from which the doctor has to make his selection, is listed in Fig. 313. The foreseeable tendency of frequent therapy repetitions at home is supported and favored by the already initiated serial production of oxygen selector apparatuses [1, 7] which enrich oxygen from the atmospheric air and deliver it at flow rates that meet the demands of the therapy variants provisioned for application at home. When skilfully used (e.g. by several individuals), an apparatus amortizes quickly. For further reducing cots, the possibility of leasing is being considered. In the future such separators will become durables which can everybody afford.

For oxygen delivery from pressure cylinders applicable at home, a certain progress can be observed. Specialized firms in Europe supply appropriate equipment; further treatment variants have been designed, which consume less oxygen.

Among the O_2MT variants for domestic application the 36 h-18 day O_2MT procedure GK 4 ranks first. Its preference for deomestic or occupational application, as well as during holidays, is obvious, because it consumes much time, is hence very expensive when accomplished in O_2MT treatment centers, and gets along with physical exertion. This standard variant and its effects have been studied most thor-

PROGRAM OF THE STANDARD (3hr O_2-MULTISTEP SHORT PROCEDURE WITH LONG-LASTING EFFECT (VERSION OF MARCH 1,1988)

UNIVERSALLY APPLICABLE AND TIME-SAVING VARIANT GK3 I ADAPTED TO THE CAPACITY OF THE OXYGEN SELECTOR "PRO VITAL"

(Manufactured by Hauni Electronics GmbH, Hamburg-Bergedorf, FRG)

6 sessions of 30 min each within 3 days, mask applicator with storage balloon, respiratory minute volume (RMV) adjusted to the capacity of the "PRO VITAL" selector by appropriate choosing of the physical exercise; due to the low exertion almost always applicable even to weakened patients, also suitable as single treatment before or after excessive stress

SESSION (SESSION UNIT)

1st step
30 min. before start of procedure 1 tablet OXYGENABUND (30 mg vitamin B1, 75 mg Dipyridamol, 100 mg Mg-orotate); if desired, 1g vitamin C can be added

2nd step
Throughout each session (30 min) O_2-inhalation through mask applicator with storage balloon supply with 7.5 l O_2/min from a „PRO VITAL" selector or up to 15 l/min

3rd step
Good circulation ensured by suitable physical exertion (20-40 watts) acc. to the patients fitness (RMV = 12-17 l/min)

Obligatory supplement
In the intervals between sessions and after end of procedure suitable exercise (often progressive) and energetic life style e.g. increase pulse to 180-age for 10 min. daily

IMMEDIATE MEASUREMENT — STARTING VALUES BEFORE THERAPY, FOR DIAGNOSIS [2]

1st session	①	O_2≋	♥	•
2nd session	①	O_2≋	♥	•
3rd session	①	O_2≋	♥	•
4th session	①	O_2≋	♥	•
5th session	①	O_2≋	♥	•
6th session	①	O_2≋	♥	•

CONTINUED PERMANENTLY [3] — CONTINUED PERMANENTLY [3]

THERAPEUTIC RESULT: MEASUREMENT APPROX 2 DAYS AFTER END OF THERAPY PROCEDURE [2]

FOLLOW UP: MEASUREMENTS AFTER MONTHS TO YEARS TO ESTABLISH WHETHER A REPETITION OF THE PROCEDURE IS NECESSARY. [2]

[1] or 9 sessions of 20 mins each within 4 1/2 day

[2] Measurement of the arterial oxygen partial pressure ($pO_{2\text{-art}}$) in the capillary blood from the ear lobe (after arterialization and 10 mins rest) at the same time of day (sober, no coffee tea etc.) using the special pO_2-meter MO 10 (manufactured by VEB Präcitronic Dresden GDR). If possible, measure PWC the value of which is more predicative

[3] Daily intake of oxygenabund 30 min before exercise training (decrease of $pO_{2\text{-ven}}$)

Long-term effects after end of procedure: Increased resting $pO_{2\text{-art}}$; decreased resting $pO_{2\text{-ven}}$; increased resting values of η, O_2-uptake and CO_2-production, therefore lasting improvement in O_2-status (energy status) of the body. In order to trigger the effects of O_2-multistep immunostimulation GK3-II (reduced susceptibility to disease or radiation damage, decreased probability of cancer when annually repeated once) each session should be supplemented with the dose of 3 thymus dragées, e.g. Thym-Uvocal (Dr. Kurt Mulli D-7844 Neuenburg, Otto-Hahn-Str. 2, FRG).

Fig. **314** Program of the standard 3 h oxygen multistep therapy short procedure with long-lasting effect (version of March 1, 1988)

oughly [7]. In accordance with the experience collected up to now, this variant seems to be of the highest efficacy as compared to the other modifications. When O_2-sparing breathing masks with storage balloons are used, one oxygen selector "ProVital" (manufactured by Hauni Electronics GmbH, Hamburg-Bergedorf, FRG) can sufficiently supply two persons with oxygen at the same time [1].

Only few variants of the O_2MT and the oxygen multistep immunostimulation are suitable for use at home. As to that, these are the variants that get along with very low physical exertion (20–40 watts or less). Physical activities of this low intensity are common in daily life (walking ≙ 25 watts; step-climbing), and can therefore be expected of all still reasonably mobile individuals.

In this context the reader should remember that hundreds of thousands of fitness instruments, such as treadmills, cycle ergometers, weight-lifting machines etc. are in private use all over the world. The risk of overstrain by such devices is greatly reduced when oxygen is concomitantly applied (O_2MT!).

A variant specially designed (also) for use at home is the 3 h-O_2MT short procedure GK 3-I, the programming of which is given in Fig. **314**. In this variant the physical exertion is limited to 20–40 watts, and hence is also easily applicable to debilitated patients. The increased respiratory minute volume resulting at this low effort is conveniently covered by the "ProVital" oxygen selector. Of very practical significance is the low expenditure of time of this broadly applicable version (3 h divided into 6 or 9 treatment units; 1/12 of the duration of the 36 h-18 day procedure). The simplest way to accomplish this O_2MT variant at home is shown in Fig. **315**. The physical exercise is accomplished by repeatedly climbing one step; a bicycle ergometer or any other technical equipment is unnecessary. For more recent results on the increase of physical and mental fitness after O_2MT, the reader is referred to [33–36].

Fig. **315** The simplest way to accomplish the 3 h oxygen multistep therapy short procedure GK 3-I at home using the oxygen selector "ProVital", manufactured by Hauni Electronics GmbH, Hamburg-Bergedorf, FRG. Low exertion by climbing up and down one step. At a step height of 17 cm and a body mass of 70 kg, 9 steps for 20 watts and 18 steps for 90 watts are to be climbed per minute

9. The oxygen multistep therapy contributes twofold to the restoration of the performance status critically reduced at very old age. Foundation of the prospects to prolong human life

In conclusion, the fateful significance of frequent and timely repetition of O_2MT applications at home, combined with properly adjusted, regular physical exercises for people at old age (over 70) should be addressed. The rapid decline of the mechanical performance reserves at the age over 70 is, as shown in Fig. **316**, the primary cause for the fact that man does not reach the genetically programmed age of about 120 years and that physical and mental powers as well as quality of life and vigor reduce much earlier [3]. A concrete perspective to delay this development, i.e. to prolong human life by about 1.5 decades, consists in the frequent repetition of the O_2MT in old age, combined with adjusted, regular physical exercise. Two important facts substantiate this prospect: performance and power reserves in very old age are no longer sufficient for physical exercises, which could improve the energetic status; just for weakened, very old people, O_2MT results in remarkable per cent gain in energy.

The oxygen multistep therapy improves the energetic situation in two ways. It significantly increases the critically reduced performance status and provides, just by means of this increase, the conditions for regular, physical training in old age, further improving the energetic situation.

Summary

After a discussion on the importance of energy and lack of energy for the human organism, the fateful decrease of the human performance reserves (physically expressable in watts) is depicted. The following considerations on the human organism and life from an energetic point of view deal with the consumption of energy by diseases and stress and with the gain in energy by physical exercises and oxygen multistep therapy. The long-lasting energetic gain, achieved by this therapy, effects the improvement of numerous physiological parameters, which can objectively be measured. There have been few therapies in the history of medicine, where it was easier to prove their positive action by measuring numerous parameters. Since energy is the prerequisite of all living processes, the oxygen multistep therapy, which reduces or even eliminates the lack of energy, is of unusual universality and yields outstanding clinical results in different branches, such as combatting angina pectoris, dyspnea, hypertension, hypotension, circulatory disorders, liver diseases, impaired vision, cancer etc. Under the form of the variant "oxygen multistep immunostimulation" the long-lasting elevation of the energetic status is combined for the first time with the action of immunomodulators. This combination results in an increase of the number of cancer cells destroyable by unspecific defense mechanisms by a factor of 10^5. The consequences of this progress to several concepts for reduction of metastasis, for increasing the effect of conventional cancer therapies and for cancer prevention are discussed. Practical details are dealt with, such as timing for treatment repetitions, treatments at home at reasonable costs, the choice of the individually best fitting treatment variant, etc.

Finally, it is outlined that the rapid decline of the performance reserves at age over 70 can be retarded by repeated O_2MT treatments combined with adjusted, regular physical exercise. The resulting improvement of the energetic situation opens the perspective of the prolongation of human life by about 1.5 decades, to which the oxygen multistep therapy contributes twice; it restores not only the performance level, critically reduced in the last period of life, by a remarkable percentage but forms also, just by this increase, the conditions for regular physical training in old age, further improving the energetic status.