Z. Rechtsmedizin 71, 79—90 (1972)

Übersichtsreferat — Review Article

Clinical and Medico-legal Aspects of Hyperbaric Oxygenation

Endre Somogyi

Institute of Forensic Medicine, Semmelweis University, Medical School, Budapest (Hungary)

Received February 14, 1972

Summary. Hyperbaric oxygenation as a therapeutic procedure gained considerable popularity during the last decade. It is increasingly applied to severe cases of respiratory and circulatory diseases as well as to cases of poisoning such as with carbon monoxide and cyanide, and in the course of radiation and tumor therapy. The limitations of the method involve not only technical but also physiological factors. Apart from caisson-disease, oxygen toxicity is the most frequent complication. Oxygen toxicity may result from extreme increase of oxygen saturation or air pressure. The sensitivity to oxygen depends to a large extent on the age of the patient and the presence of diseases. The effect of hyperbaric oxygenation is measurable experimentally. Detailed experimentation is indicated prior to clinical application by this method. Widespread application of hyperbaric oxygenation requires detailed investigation of related clinical and morphological problems from a medico-legal aspect.

Zusammenfassung. Die Sauerstoff-Überdruckbeatmung hat in den letzten Jahrzehnten stark an Bedeutung gewonnen. Sie findet zunehmend Anwendung bei der Behandlung von schweren Erkrankungen der Atmungsorgane, bei Herz- und Kreislauferkrankungen, die zu einer Sauerstoffinsuffizienz des Gewebes führen, bei Vergiftungen, die den Sauerstofftransport und die Gewebsatmung betreffen (CO, Cyanid), bei der Strahlentherapie und Tumorbehandlung. Die neben der Caissonkrankheit vorkommenden Komplikationen, pathologische Veränderungen der oberen Atemwege und des Lungenparenchyms sowie zentralnervös bedingte Symptome, lassen sich auf die bei extremer Erhöhung der Sauerstoffsättigung bzw. des atmosphärischen Drucks (1,5—2,0 atü), aber auch bei Langzeitbehandlung auftretende Toxicität des Sauerstoffs zurückführen, wobei der Intoxikationsmechanismus noch unbekannt ist.

An Ratten wurde die therapeutische Wirkung der Sauerstoff-Überdruckbehandlung an der experimentellen Gangrän untersucht. Durch einen Elektroschock (190 V für 8 sec) wurden Gefäße und Nerven der Beinmuskulatur geschädigt, was zu einer Gangrän, bei 80% der Tiere innerhalb von 6 Tagen und bei allen Tieren innerhalb von 10 Tagen zu einem Verlust des Gliedes führte. Bei gleichzeitiger Anwendung von Sauerstoff-Überdruckbehandlung konnte bei 20% der Tiere ein Abklingen der Gangrän bewirkt werden, das betroffene Glied blieb erhalten, während bei weiteren 20% der Tiere die nekrotischen Prozesse deutlich verlangsamt waren. Es scheint dabei die Verbesserung des Gewebsstoffwechsels sowie die Hemmung bestimmter Enzymsysteme durch Sauerstoff von Bedeutung zu sein.

Auf die mit der zunehmenden Verbreitung der Sauerstoff-Überdruckbehandlung verbundene rechtsmedizinische Problematik, Komplikationen, Fragen der Indikation wird hingewiesen.

Key word: Hyperbaric oxygenation, clinical and morphological problems.

Introduction

The hyperbaric oxygenation is a rediscovered subject of medical research of the last decade. The field of its application becomes more and more extended, the observations obtained are variable and frequently contradictory. However, its application in both experimental and clinical practice will surely be more frequent in the future.

The alterations of the internal and external respiration as well as of the oxygen transport force often the physician to increase the oxygen tension for shorter or longer periods of time in order to avoid the damages of hypoxia. The experimental and clinical observations allow us to conclude that the hyperbaric oxygenation represents a well applicable method for the prevention of hypoxic damages.

All the methods of therapy have some properties apart from their positive characteristics, limiting their applicability. These problems are usually recognized during the wide application of the methods.

The present paper concerns the problems appearing during the use of hyperbaric oxygenation. We hold as necessary to describe our observations obtained by chemical and experimental investigations of hyperbaric oxygenation and to compare with those of others.

The History of Hyperbaric Oxygenation

Boerema *et al.* [9] called his paper "Life without blood" in 1959, concerning the theoretical basis of hyperbaric oxygenation and his observations. The application of hyperbaric oxygenation (HBO) for therapeutic purposes is not new, nevertheless, Boerema is considered as the modern pioneer of it. The problem of HBO has become extremely far-reaching. Numerous papers are being published, therefore, the detailed review of literary data is beyond the scope of the present paper. Nevertheless, a brief survey should be made.

The industrial and marine application of hyperbaric air dates back in ancient times. These data are reviewed by summarizing works: Besznyák [6], Fontaine [17] and Matthys and Bühlmann [29].

The application of hyperbaric air for medical purposes in 1662 is associated with the name of Hensaw [18]. He applied a chamber for the treatment, which was equally suitable for both hyperbaric and hypobaric intervention. He used hyperbaric air in the acute and hypobaric one in the chronic diseases. This method did not come into general use and the "hyperbaric medicine" did not let hear from itself until 1834—1838. Junod [26] constructed a chamber for the patients where hyperbaric air was produced. This was used for the treatment of cerebral diseases. This was the beginning of the wide application of hyperbaric oxygen therapy in Europe. Fontaine [17] built a hyperbaric operating room where together with his assistant Pean made 27 operations during several months. They observed first that cyanosis and asphyxia did not appear during such operations. Fontaine himself made operations and fell victim to an accident in his institute. Bert [5] treats in detail the physiological alterations connected with the HBO treatment. Cunningham built a 5 storied hyperbaric hospital, each floor of which had 12 rooms. He treated here diabetes, syphilis and carcinoma, since according to his opinion, anaerobic infections played some role in the development of these diseases. The recent 30 years have an extremely large literature which will be concerned when interpreting the most important results.

The Theoretical Basis of the Hyperbaric Oxygenation

The oxygen content of the air is 20.9%, this is the usual atmosphera. However, from a biological point of view, not only the oxygen concentration but also the oxygen tension is of importance. At a pressure of 735 mm Hg (1 Atm = 1 kg/cm^2 = technical atmosphere) the partial pressure of oxygen amounts 0.2 part of the air pressure. The increase of oxygen pressure can be achieved either by the increase of its concentration or by that of the total pressure of the air. At a total pressure of 5 Atm we can reach the same partial pressure of oxygen, about 1 Atm, as at a normal pressure and 100% oxygen saturation. The blood binds oxygen in two forms: bound chemically to hemoglobin and dissolved physically in the plasma. Under normal circumstances the oxygen bound chemically is more important. Respiring air at a pressure of 1 atmosphere, the oxygen content of the arterial blood of healthy people in a state of rest amounts about 20 vol% in the case of complete saturation and this value cannot be increased. The amount of oxygen dissolved physically in the plasma is not significant under normal circumstances, it is equilibrated with the oxygen tension of the alveolar air. As a consequence, the change of the oxygen tension in the alveoli induces the amount of oxygen dissolved physically in the plasma. Respiring air at 1 Atm, the amount of oxygen dissolved in the plasma is about 0.3 vol%, whereas, breathing 100% oxygen at a pressure of 1 and 3 atmospheres it reaches 2 and 6 vol%, respectively. Theoretically this amount of oxygen is sufficient for the covering of oxygen requirements of a normothermic organism in state of rest. At the same time this offers a possibility to be cut off from the chemical transport of oxygen by hemoglobin. Thus the HBO seems to represent an easily realizable, painless therapeutic procedure suitable for the therapy of certain hypoxic, ischemic states. However, the question seems to be so simple only theoretically. The clinical application needs wide experimental investigations.

The Practical Realization of HBO

For experimental and clinical realization of HBO a so-called hyperbaric chamber is essential. It is a system constructed from transparent walls and to be closed hermetically, offering a possibility for realization of the pressure necessary and the other conditions required by the experiments or therapeutic procedure. The sizes of the chamber depend on their application. There are experimental chambers of 100 ml volume and large ones consisting of several rooms admitting complete operating teams. The large chambers of special designation are extremely expensive and their running needs special measures. The violation of these rules may involve serious danger.

In the case of observance of rules the HBO represents no significant danger for the healthy organism. This is supported by the results of the large hyperbaric centers where no damage of the personnel was observed even during large number (several thousands) of treatments. However, the characteristics of the HBO therapy involve that some patients suffering from certain diseases can endure the treatment much worse. Thus e.g. acute catarrh of the upper respiratory tract, disease of the labyrinth, dental caries may cause unpleasant pains during the compression in the teeth and ear, or a sense of suffocation. Therefore, the investigation of the patient and the personnel is necessary in this direction before the starting of the treatment. In the case of senseless patients the failure of equilibration of pressure difference between the tympanic cavity and the environment may lead to the hemorrhage or even rupture of the tympanic membrane, since in the absence of indication of the pain the HBO therapy is continued. This may result organic alterations involving juristic consequences toward the personnel performing the treatment.

The Application of HBO and the Problems of It

The fields of application of HBO can already be defined on the basis of results of the large hyperbaric centers.

The indication field of HBO is as follows [29]:

a) Disorders of the external respiration, atelectasia, pneumonia, lung edema of cardial or extracardial origin, chronic bronchitis, asthma bronchiale, pulmonary embolism, neonatal insufficiency of respiration.

b) Circulatory disorders affecting the oxygen transport, acute myocardial infarction, shock, chilblained disorders, combustions, traumatic ischemia, thromboses, embolisms, acute hemolysis, inactivation of hemoglobin.

c) Non-primary ischemic disorders of the internal respiration, cyanide intoxication, CO intoxication.

d) Further fields of application, irradiation of tumours, maintenance of organ transplantate.

The HBO therapy has successfully been applied in all these fields. The results will be concerned shortly later. First of all attention should be called to the problems and difficulties observed during the application of HBO therapy. The increase of oxygen tension up to a certain level, e.g. 1.5—2.0 Atm induces clinical symptoms even during a short period of time. A special group of questions arises on the basis of the fact that the average value of oxygen pressure must not be increased over 0.3—0.5 Atm during prolonged HBO treatment of several weeks.

The cellular enzyme systems are inhibited by the oxygen pressure higher than the normal one [3, 19, 35]. The endothelial cells seems to be especially sensitive, their damage increases the streeming out of the liquid into the interstitial space, making longer the way of diffusion of the respiratory gases [20, 32, 37].

In connection with the HBO therapy the individual factors should also be considered, e.g. new-born and little children display a much higher sensitivity of the pulmonary parenchyma to the high pressure than the adults. However, in the case of the latter, a chronic pulmonary disease of long duration or an acute one may increase the sensitivity to oxygen to a great extent. It is known that the artificial oxygen respiration is not harmful for the lungs and the respiratory tract in adults even if it is maintained for several weeks, on condition that the rate of oxygen does not exceed 60% at a normal pressure. States of grave hypoxia as well as pulmonary edema appearing at the beginning of pulmonary processes, such as influenzal pneumonia, lipid embolism or respiratory injuries, can well be influenced. The investigations seemed to prove that a higher oxygen percentage is not necessary in most cases and its application induces toxic symptoms. The symptoms of oxygen intoxication can be divided into 3 large groups: a) Symptoms of the upper respiratory tract; b) Symptoms of the pulmonary parenchyma; c) Symptoms of the central nervous system.

The exact pathomechanism of the oxygen toxicity is unknown, it manifests itself in form of epileptic convulsions and pulmonary edema. Its pathological basis is presumably formed by the alterations of the lungs and the central nervous system. The respiration of high concentration of oxygen for a long period plays a role in the appearance of it.

Apart from the oxygen toxicity, the caisson-disease as well as the fire and explosion represent the most frequent dangers of the HBO therapy. However, these can be avoided using a suitable decompression and safety rules.

Some Fields of Application of HBO

According to the clinical experience, the most favourable field of application of HBO is the cardial surgery. It is used with good results first of all in the surgical solving of congenital heart failures and diseases accompanied by cyanosis. There are reports on good results in several hundreds of cases of Fallot's tetralogy, transposition of the great vessels and pulmonary atresia [13, 30, 31]. The advantages of the therapy originate in the better oxygenation of the seriously hypoxic tissues, the oxygen demand is decreased by the hypothermia, whereas the HBO increases to a great extent the amount of oxygen being at disposal in the tissues. One of the most significant results of the HBO during the cardial operations is the suppression of the ventricular fibrillation occurring as a consequence of hypothermia rather frequently. This eliminates often a complication involving the collapse of circulation.

The experimental mortality was decreased to a significant percentage by the HBO therapy after the ligature of coronary vessels of rabbits [1, 2, 4, 27, 30, 38]. These experimental observations have been reproduced even in human cases of coronary insufficience and the mortality was also decreased.

Apart from some clinical cases, we have rather experimental observations as regards the HBO treatment of cerebral hypoxia and shock. Nevertheless, these results are promising for the future to offer an efficient therapeutic method against the above syndromes.

One of the most fruitful fields of the HBO therapy is the treatment of anaerobic infections where it has successfully been used by numerous authors [10, 31]. The results are very good in the case of Clostridium perfringens infections. Conspicuous improvement and what is more, recovery was achieved in the therapy of otherwise fatal gas gangrene. However, it should be noted that in the case of the other frequent anaerobic infection, the tetanus, the value of the HBO therapy was lower than expected.

One of the most indisputable fields of the HBO therapy is the treatment of CO intoxication. The HBO therapy seems to surpass the possibilities and therapeutic effects of all the procedures having been applied so far [33].

The HBO therapy has recently been applied also in the pediatrics; it has been introduced for the treatment of asphyxia neonatorum and so-called hyaline membrane disease. One can expect good results from this method even in cases of embryonic hypoxia and anoxia where the cutaneous respiration supposingly may play some role [21].

The anticarcinogenic effects of X-ray and radium irradiations increase proportionally with the increase of oxygen tension. This observation forced the scientists to carry out the irradiations in hyperbaric chambers. The clinical observations seem to support the existence of the effect supposed [6, 7].

Apart from the above examples, numerous fields could be listed, such as the cyanide intoxication, acute circulatory insufficience, conservation of materials of transplantation, etc. [7, 8, 15]. Naturally, the clinical application should be preceeded by suitable experimental observations.

Own Experimental Observations on the Effect of HBO

It was observed during the electropathologic investigations of our Institute that the electric shock performed in the crural musculature of rats was followed

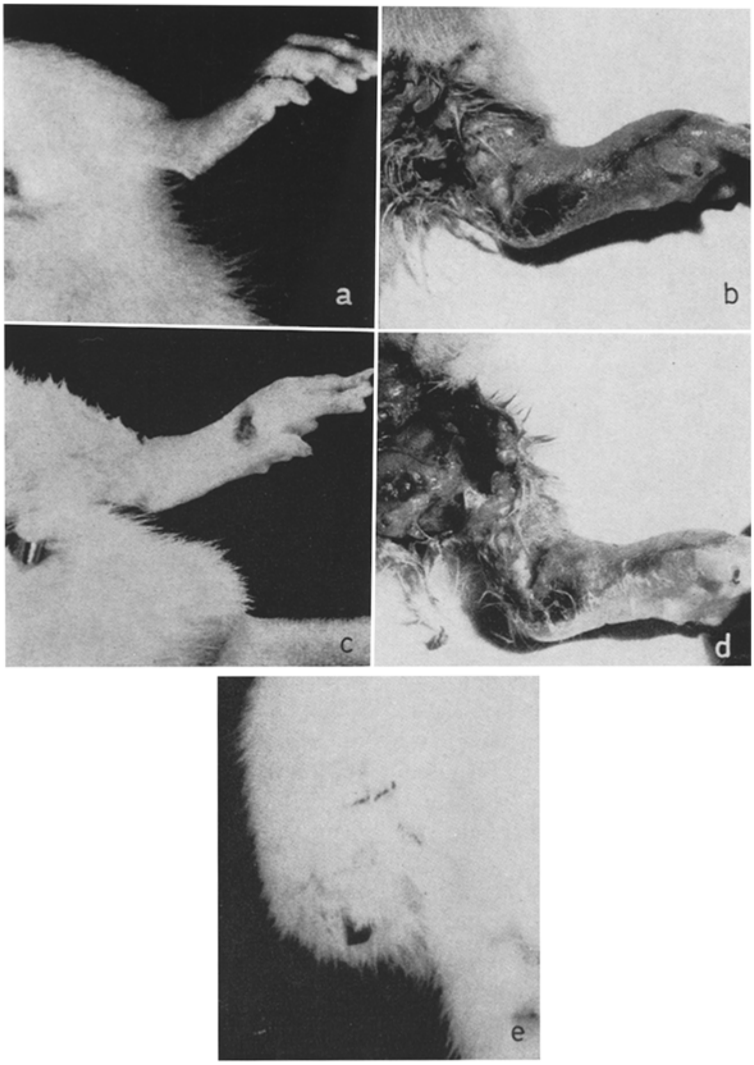

Fig. 1. a The limb of the rat after the electric shock. b Note the ulceration of the limb 3 days after the electric shock. c The limb of the animal is edematous and swollen 6 days after the electric shock. d Note the progressive gangrene on the limb of the animal, 8th day. e The limb is mutilated on the 12th day, a stump indicates its place

in a significant number of cases by gangrene of the limb causing later the loss of it (Fig. 1). The investigations revealed that the electric shock caused the damage of the arteries, venes and nerves of the femur explaining the reasons of the alteration (Figs. 2 and 3).

Acute peripheric circulatory disorder often occurs in the clinical practice. If the suitable treatment fails, the limb is more or less heavily damaged or may be lost. The reconstructive and desobliterative interventions of the vascular surgery as well as the applications of fibrillolytic substances have made better the prognosis of the treatment, however, in spite of

Fig. 2. Arteriographs indicating the normal (left-sided) and electrically shocked (right-sided), obliterated vessels. b The arteriograph of the mutilated limb shows an obliterated artery at the height of the damage

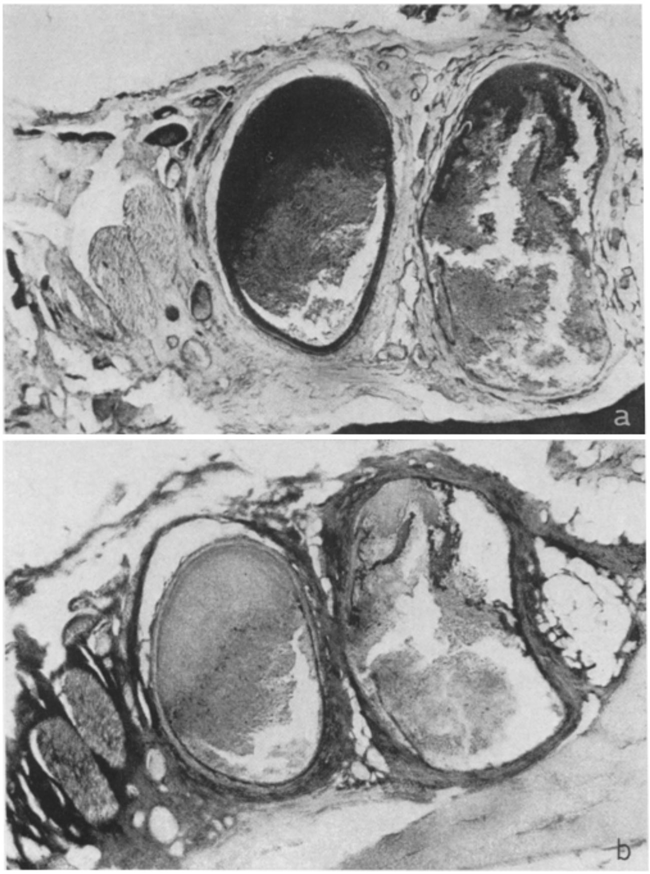

Fig. 3. a The necrosis of the arterial and venous walls and the thrombosis of the lumen can be seen at the height of the electric shock. Phosphotungstic acid-hematoxylin-eosin staining. b The necrosis of the muscle cells as well as the changed staining properties of the muscle and connective tissue of the environment is shown by Mallory's trichrome staining

that the problem of therapy cannot be considered as solved at all. The elaboration of new methods and operative procedures, application of new medicaments offering a possibility to improve the results, are justified by all means. The experimental testing of there constructive operations and new therapeutics represent a difficult task, first of all because of the difficulties of standardization of the acute circulatory disorder in most of the experimental animals. The induction of experimental arterial and venous thrombosis has been concerned by numerous papers [11, 12, 14, 16, 22—25, 28, 29]. However, the practical introduction of the methods revealed that the circulatory disorder cannot be produced in every case representing a serious difficulty of standardization of the methods.

In our own experiments the gangrene of the limb was surely brought about by 190 V of 8 sec duration, therefore these parameters offer a possibility of standardization. We are aware of the fact that damages of similar origin occur relatively rarely in the clinical practice. The circulatory disorder which seems to be isolated clinically (arterial and venous thrombosis, embolism) can often be considered as of arterial or venous origin only at the beginning of the process. Later on parallel with the propagation of the process a trophic disorder originating in the incomplete nutrition of the limbic nerves may complicate the situation. The reactive and compensatory ability of circulatory system of rats differs although from that of the man, our method seems to be suitable for investigations of certain acute peripheric circulatory disorders under experimental conditions.

There are various methods at disposal for the treatment of damages following the acute peripheric circulatory disorders. The irreversible damage of tissues based on the grave hypoxia plays a primary role in the development of limbic gangrene coming into being as a consequence of arterial occlusion. Therefore, the idea was plausible that the increase of oxygen content of the blood for which the HBO therapy offers a possibility, must be advantageous. Collaborating with the 4th Clinic of Heart and Vascular Surgery, Semmelweis University Medical School, Budapest, we attempted to prevent the development of experimental gangrene (Fig. 4). The experiments have revealed that 80% of the control animals lost the damaged limb by the 6th day and the limbs were mutilated in all the animals by the 10th day subsequent to the electric shock. The necrosis and mutilation of the animals treated with HBO was of much slower speed, by the 6th and 10th days 25% and 60%, respectively, showed a necrosis of the limb. The limb was saved in 20% of the treated animals definitely, whereas, in another 20% of them, the duration of the complete necrosis of the limb could be significantly lengthened, which perhaps may offer some possibilities for the application of other therapeutic interventions (Fig. 5). The effect of HBO in our experimental material can be explained by the decrease of oxygen consumption of tissues, the inhibition of activities of certain enzyme systems as well as by the improvement of the metabolism of tissues (Fig. 6). The conclusion can definitely be drawn that the necrosis takes place much slower in the animals treated with HBO, which gives more advantageous possibilities for application of other surgical or pharmacological therapies.

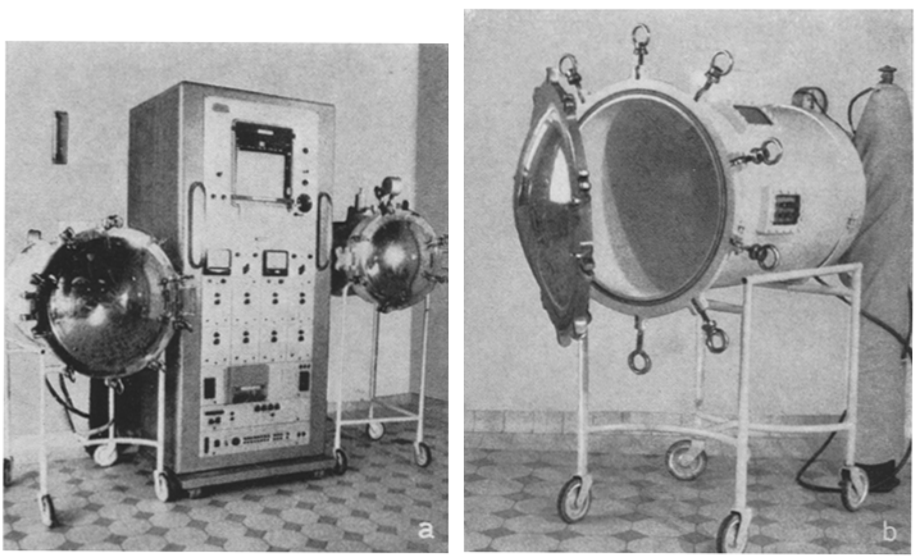

Fig. 4. a Hyperbaric oxygen chamber and registrating apparatus. b A simple, well applicable variant of the hyperbaric chamber

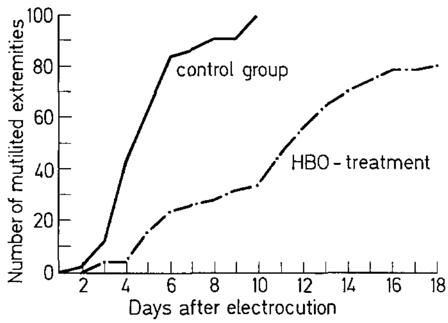

Fig. 5. The diagram indicates in percentage the rate of recovery of the limbs of animals treated with HBO

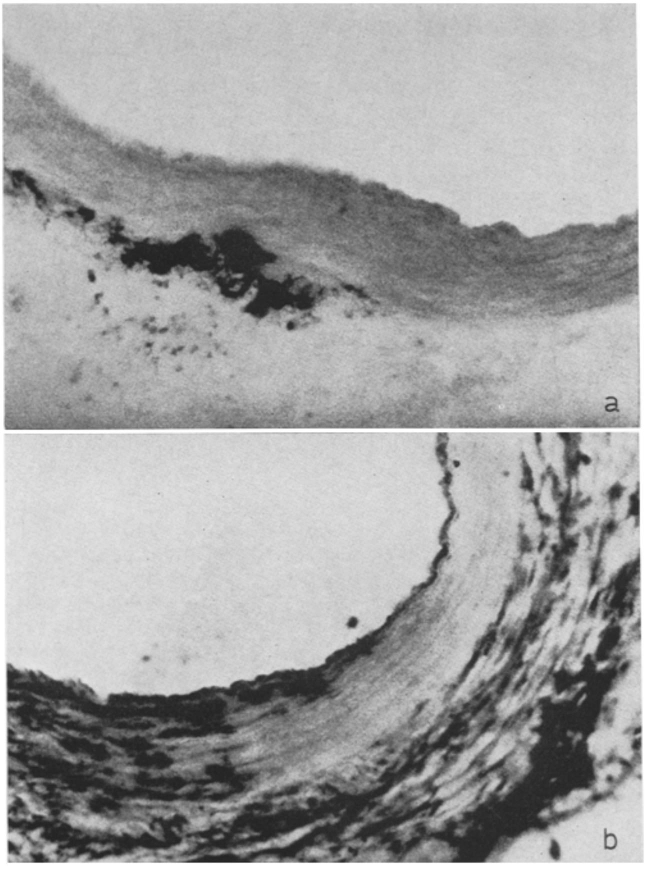

Fig. 6. a The HBO treatment induces the appearance of a network of alkaline phosphatase at the border of media and adventitia. Naphtol AS-phosphate method. b A regenerated intimal layer displaying aspecific esterase activity appears above the damaged media. Naphtol AS-acetate method

The Forensic Medical Problems of the HBO Therapy

The experimental and clinical results seem to prove undoubtedly that the HBO therapy represents a good method coming more and more into general use and giving good results in many fields of the medical practice. Of course, the method has some own limitations and strong fields of indication. However, it seems to be necessary for the forensic medicine, parallel with the publicity of this method, to study in detail it as a new therapeutic process and to take a stand on the questions being open yet. The thorough examination of the problems of the HBO therapy can offer a basis for the experts in forensic medicine to be able to take a stand in the questions arising during the application of HBO therapy. This involves not only the cases taking place as consequences of non-observance of the strict technical rules of application of the HBO treatment, but also those arising from the indications being not enough cautious. As every new therapeutic method, it propagates widely at the beginning and the criticism against the method elaborates later the real fields of indication. Thus the forensic medicine may contribute to the correct indication of the method by detailed investigation of the problems of the procedure.

The trends of research in forensic medicine have undergone significant changes during the last decade. The detailed analysis of the morphological problems connected with the HBO therapy created a possibility during our experiments to obtain own experience being of practical importance for the clinicians. We are of the opinion that our experimental results and the possibility of their application well demonstrate the change of connections having been formed recently between the clinicians and the experts in forensic medicine.

References

1. Alister, Mc., Stark, I. M., Norman, I. N., Ross, R. M.: Inhibitory effects of hyperbaric oxygen on bacteria and fungi. Lancet **1963 I**, 1040.
2. Alter, S., Esmond, W. G., Cowley, R. A.: Hyperbaric oxygenisation in vascular collapse. J. thorac. Surg. **44**, 759 (1962).
3. Balogh, K., Jr.: Dihydrolipoic dehydrogenase activity: A step in formation of acyl-coenzyme A, demonstrated histochemically. J. Histochem. Cytochem. **12**, 404 (1964).
4. Barclay, R. S., Ledingham, I. McA, Norman, I. N.: Experimental and Human Cardiac Surgery with Hyperbaric Oxygen. In: Boerema, I., Brummelkamp, W. H., Meijne, N. G., Clinical Application of Hyperbaric Oxygen. Amsterdam-London-New York: Elsevier 1964.
5. Bert, P.: La pression barométrique; recherches de physiologie experimentale. Paris: Masson 1878.
6. Besznyák, I.: Application of hyperbaric oxygenation in the medicine (Hungarian). Orv. Hetil. **108**, 193 (1967).
7. Besznyák, I., Sebestyén, M., Nemes, A.: Wirkung der hyperbaren Sauerstofftherapie auf die Ergebnisse der Degranol-Behandlung von experimentellen Geschwülsten. Arch. Geschwulstforsch. **30**, 109 (1967).
8. Besznyák, I., Somogyi, E., Nemes, A., Sebestyén, M., Sótonyi, P.: Treatment of experimental limb-gangrene with hyperbaric oxygen (Hungarian). Morph. és Ig. Orv. Szemle **8**, 52 (1968).
9. Boerema, I., Meyne, N. G., Brummelkamp, W. H., Bouma, S., Mensch, M. H., Kamermans, F., Stern, H. M., Aaldaren, W.: Life without blood. Arch. chir. neerl. **11**, 70 (1959).
10. Brummelkamp, W. H.: In: Boerema, I., Brummelkamp, W. H., Meijne, N. G., Clinical Application of Hyperbaric Oxygen. Amsterdam-London-New York: Elesevier 1964.
11. Cotran, S. R.: On the presence of an amorphous layer lining vascular endothelium under abnormal conditions. Invest. **14**, 1826 (1965).
12. Cotran, S. R.: The delayed and prolonged vascular leakage in inflammation. An electron microscopic study of the vascular response after thermal injury. Amer. J. Path. **46**, 589 (1965).
13. Cunningham, O. J.: Oxygen therapy by means of compressed air. Anesth. Analg. Curr. Res. **6**, 64 (1927).

14. Deaton, H. L., Anlayn, W. G.: A study of experimental methods for producing thrombosis in small arteries. Surg. Gynec. Obstet. **11**, 131 (1960).
15. Ewans, W. E., Drain, I. C., End, E., Ellison, E. H.: The use of hyperbaric oxygen in the treatment of endotoxin shock. Surgery **56**, 184 (1964).
16. French, I. E., Poole, I. C. F.: Electron microscopy of the platelets in artificial thrombi. Proc. roy. Soc. B **157**, 170 (1963).
17. Fontaine, J. A.: Amploi chirurgicale de l'air comprimé. Un. Medic. **28**, 448 (1879).
18. Hensaw, J.: Cit.: Jacobson, J. H. I., Morsch, J. H. C., Rendell-Baker, L.: The historical perspective of hyperbaric therapy. Ann. N.Y. Acad. Sci. **117**, 651 (1965).
19. Harrison, G.: Lung ultrastructure effects of breathing oxygen at 0,6 atm for 90 days. J. Cell Biol. **39**, 58 (1968).
20. Hughs, I.: Ultrastructure of the air-treating organs of some lower vertebrates. VII. Int. E. M. Congress, Grenoble, Vol. **3**, 599 (1970).
21. Hutchinson, J. H., Kerr, M. M., Williams, K. G., Hopkinson, W. I.: Hyperbaric oxygen in the resuscitation of the newborn. Lancet **1963 I**, 1019.
22. Hüttner, I., Jellinek, H., Kerényi, T., Szemenyei, K.: Fibrinoid necrosis of the vessel wall induced by acid painting (Hungarian). Morph. és Ig. Orv. Szemle **5**, 91 (1965).
23. Hüttner, I., Jellinek, H., Sótonyi, P., Tóth, A., Makói, Z.: Enzyme histochemical investigations on the regenerating aorta in animal experiments (Hungarian). Morph. és Ig. Orv. Szemle **5**, 12 (1965).
24. Jellinek, H., Szemenyei, K., Kerényi, T., Hüttner, I.: Alterations of small arteries observed after acid painting (Hungarian). Morph. és Ig. Orv. Szemle **5**, 88 (1965).
25. Jellinek, H., Szemenyei, K., Kerényi, T., Hüttner, I.: Effect of painting with acid on muscular type small arteries. Acta morph. Acad. Sci. hung. **14**, 165 (1966).
26. Junod, V. T.: Recherches physiologiques et thérapeutiques sur les effets de la compression et de la reréfaction de l'air, tant sur le corps que sur les membres isolés. Rev. méd. franç. étrang. **3**, 350 (1934).
27. Lélek, I.: Effect of hyperbaric oxygenation on the mortality following the ligature of the coronary artery (Hungarian). Orv. Hetil. **109**, 691 (1968).
28. Martin, M.: Thrombusbildung in Tierexperiment. Vital, licht- und elektronenmikroskopische Befunde. Zbl. Phlébologie **6**, 942 (1967).
29. Matthys, H., Bühlmann, A. A.: Erfahrungen mit der hyperbaren Sauerstoffeinwirkung beim Menschen. Schweiz. med. Wschr. **100**, 13 (1970).
30. Meijne, N. G., Bulterijs, A. B., Schoemaker, G., Eloff, S. J. P.: Treatment of dogs with oxygen under high atmospheric pressure, after ligation of the descending branch of the left coronary artery. Dis. Chest **44**, 234 (1963).
31. Moon, A. J., Williams, K. G., Hopkins, W. J.: A patient with coronary thrombosis treated with hyperbaric oxygen. Lancet **1964 I**, 18.
32. Pascale, L. R., Wallyn, R. J., Goldfein, S., Gumbiner, S. H.: Treatment of tetanus by hyperbaric oxygenisation. J. Amer. med. Ass. **189**, 408 (1964).
33. Schulz, H.: Thrombocyten und Thrombose im elektronenmikroskopischen Bild. Berlin-Heidelberg-New York: Springer 1968.
34. Sluijter, M. E.: The Treatment of Carbon Monoxide Poisoning by Administration of Oxygen at High Atmospheric Pressure. Academisch proefschrift, Amsterdam 1963.
35. Somogyi, E., Sótonyi, P., Nemes, A., Sebestyén, M., Besznyák, I.: Induction of limb-gangrene by electric current in rat (Hungarian). Morph. és Ig. Orv. Szemle **7**, 272 (1967).
36. Taheri, A. S., Mases, M. D., Stoesser, F. G.: Canine heart storage under hyperbaric and hypothermic conditions. Angiology **19**, 573 (1968).
37. Trapp, W. G., Creighton, R. C.: Experimental studies of increased atmospheric pressure on myocardial ischemia after coronary ligation. J. thorac. cardiovasc. Surg. **47**, 687 (1964).
38. Williams, R. D., Carey, L. C.: Studies in the production of "standard" venous thrombosis. Ann. Surg. **149**, 381 (1959).

Prof. Dr. E. Somogyi
Institute of Forensic Medicine
Semmelweis University Medical School
Budapest IX., Üllöi ut 93.
Hungary