Summary

The evolution of the recognition and treatment of diving-related illnesses is traced over the past 150 years. Improvements in morbidity and mortality began with the introduction of standard air treatment tables by the U.S. Navy. Following a historical recommendation and limited practical experience that oxygen may be beneficial, the U.S. Navy produced treatment tables which were in common use until about 20 years ago when further research produced minimal recompression oxygen tables that revolutionized conventional treatment. Concurrent advances in pathophysiological knowledge have resulted in a better understanding of the disease and a logical application of therapeutic agents. Recent research has implicated the prostaglandin system. Therapeutic manipulation of this system has been shown to improve blood flow and promote functional recovery in ischemic neurons. This offers hope for improving the outcome of diving illnesses in those patients who fail to respond to conventional therapy.

Following the adage that prevention is better than cure, scientists of the latter part of the 19th century and the early part of this century devoted much time and effort to developing means of returning safely to atmospheric pressure after diving. Again, many theories were proposed to facilitate the safe elimination of inert gas, but the study by Boycott. Damant and Haldane led the field in prevention of decompression sickness. The concepts proposed by them still constitute the major theory behind safe decompression, although many of the factors they considered have been modified by experience and advances in knowledge of the uptake and elimination of inert gas.

Despite advances in prevention, decompression sickness continued to occur. Concurrently, the therapeutic application of air recompression also advanced from somewhat arbitrary recompressions, e.g., to the pressure of the original exposure, or to the depth of relief of symptoms. The USN Diving Manual of 1924 contained the first standard treatment tables. Although the results obtained with these tables greatly improved upon preceding methods of treatment, they were not entirely satisfactory.

Paul Bert suggested that oxygen may have therapeutic value to replace nitrogen in the body and thus treat compressed air illness. Similar recommendations were made in the early part of this century, but it was not until 1937 that Yarbrough and Behnke reported successful treatment using oxygen after oxyhelium diving. This reported success led Van Der Aue and his colleagues to develop a series of treatment tables for the USN which used oxygen when available in conjunction with air therapy. These tables were published as USN Tables 1-4. A review of the use of these tables by Rivera indicated they were an improvement on previous methods for the treatment of joint pain, but still not satisfactory for more serious cases of decompression sickness. Using minimal recompression with 100% oxygen inhalation, Goodman and Workman developed treatment tables, which were introduced as USN Tables 5 and 6 in 1961. These tables have significantly improved treatment. A retrospective study of treatments carried out in USN facilities between 1971 and 1981 showed that the correct application of the tables produced a 95.5% one-treatment success rate compared to 76% reported by Workman for USN Tables 1-4. Use of Tables 3 and 4 resulted in a 47% failure to achieve a cure on first recompression. Tables 5 and 6 have proved so effective in treatment that they are now considered the most important approach to therapy in military and civilian diving operations in most of the Western world.

Notwithstanding the great improvement in treatment these tables have brought, a certain number of diving accidents occur that do not respond to conventional pressure treatment. It has been suggested that benefit could be derived from...
advances in diving technology by submitting the patient to a saturation regime of treatment that involves extended exposures to moderate pressure, breathing high but not acutely toxic levels of oxygen. Some success has been achieved with this form of treatment, but some criticism has also been leveled at the procedure.

Along with the development of improved methods of pressure treatment, the search for therapeutic agents which can be used in conjunction with primary treatment methods has continued. During the history of treatment of DCS many therapeutic agents have been tried empirically, although new advances in the knowledge of the pathophysiological events that occur have led to a much more rational approach to treatment of the disease process. A review by Catron and Flynn covers this topic in great detail, but the essence of adjuvant therapy is fluid replacement to combat the hemoconcentration which can occur in DCS. The argument over which fluid to use continues because there are specific properties of several media that may confer theoretical advantages, particularly regarding their actions on blood viscosity and platelet function. Steroids also have a value particularly in decompression sickness of the brain and spinal cord. Their use is based on experience with other central nervous system (CNS) disorders where they are used to combat edema. Because severe decompression sickness involves complex changes to the coagulation system and blood platelets, a variety of anticoagulants and antiplatelet drugs have been tested in experiments with animals and humans. The results obtained are conflicting and do not appear to offer any substantial improvement. Nevertheless, it is probably true that the current therapeutic approach does offer benefits to the patient with severe decompression sickness, and in fact, has been used with remarkable effect even in the absence of recompression therapy.

This paper is intended to demonstrate how the complex changes which accompany decompression disorders, particularly those of the nervous system, may be influenced by the therapeutic application of substances which have been implicated in the pathophysiological process of DCS.

Bubble emboli from dissolved inert gas in the case of decompression sickness, or from alveolar gas in the circulation in the case of cerebral air embolism due to pulmonary barotrauma, tend to travel to the neuraxis. Here, they obstruct the circulation and cause ischemic cellular damage. Despite a few differences, certain aspects of the pathophysiology of these disorders are very similar to acute stroke, where the damage to the nervous system is also mediated by the ischemic cell damage that results from critical interruption of the blood supply to areas of the brain. The belief that the effects of decompression sickness may be the result of venous infarction due to stagnation of blood in the epidural vertebral venous system is relatively unimportant when the actual damage that results is ischemic. The role of autochthonous bubbles will not be discussed here because the damage which they produce may cause permanent disruption of individual cells, and can therefore be considered irreversible.

It is becoming increasingly clear that blood flow does not drop to zero in focal ischemia of the CNS, but that some collateral circulation remains. Perfusion may enter a critical range during which cellular function is suspended, but viability is preserved for many hours. Primate studies have demonstrated that considerable recovery is possible up to 16 hr after clipping the middle cerebral artery. It is important to know what factors convert a viable area of nervous tissue with suspended function into an infarct. One suggestion is that an interaction of blood and damaged tissue may release substances that increase progressively the microvascular resistance within the damaged tissue beyond the stage where it can be reversed. Consequently, a return of function is delayed to that area of tissue. Furthermore, it has been suggested that the prostaglandin system may have a role in this process.

Thromboxane A2 and PG12 are formed from precursors which are formed from arachidonic acid released from membranes. Platelet enzymes produce thromboxane A2, a potent platelet aggregator and vasoconstrictor, whereas endothelial enzymes produce PG12, a vasodilator and the most potent inhibitor of platelet aggregability known. The production pathway of these two extremely potent substances can be blocked by indomethacin, a well-known anti-inflammatory agent. PG12 has recently become available for investigation as a therapeutic substance.

The possible benefit to reperfusion following ischemic cell damage of the CNS by the therapeutic application of indomethacin and PG12 are under investigation at the Naval Medical Research Institute in Bethesda.

In an animal model of global ischemia produced by elevating the CSF pressure to the mean systemic arterial pressure for 35 min, MR1 investigators found that after 30 min of reperfusion, mean blood flows were relatively low with focal zones of extremely low flow. The infusion of indomethacin and PG12 during the recovery phase eliminated the zones of very low flow and increased appreciably the mean blood flow in gray and white matter. In addition to improving postischemic reperfusion, investigators hypothesized that the combination of heparin, indomethacin and PG12 may also promote the recovery of nerve cell function following ischemia.

Consequently, a model was developed in which neuronal function was monitored by the cortical sensory-evoked response (CSER) to peripheral nerve stimulation. Focal ischemia was produced in the right cerebral hemisphere by inducing incremental air embolism via the right internal carotid artery. Sufficient quantities of air were introduced to maintain the amplitude of the PI–N1 wave of the CSER to 10–20% of its control value for 1 hr. The same index of neuronal function was used to monitor a recovery period of up to 2 hr. A combination of PG12, indomethacin and heparin resulted in a 57% recovery relative to baseline at 60 min and 80% at 2 hr as compared to 17% recovery in untreated animals at 2 hr. Blood flow studies indicated that the combination of drugs eliminated blood flows in the “neuron-disabling” range as compared to the inefficacy of no treatment, or to combinations of drugs other than the triple administration cited above. These results suggest that the combination of PG12, indomethacin and heparin can indeed counteract the process of impaired microvascular perfusion and promote nerve cell recovery after reversible focal ischemia.

These findings offer considerable hope for the future in improving the adjuvant therapy of
decompression sickness and cerebral arterial air embolism, particularly in the small though important number of patients who respond poorly or not at all to conventional therapy.

Acknowledgements

This work was supported by the Naval Medical Research and Development Command, Research Work Unit M009901C.001. The opinions and assertions contained herein are the private ones of the authors and are not to be construed as official or reflecting the Navy Department or the Naval Service at large.

The experiments reported herein were conducted according to the principles set forth in the "Guide for the Care and Use of Laboratory Animals," Institute of Laboratory Animal Resources, National Research Council, DHEW Publ. No. (NIH) 78-23.

References