DIVER NARCOSIS, FROM MAN TO CELL MEMBRANE

Prof. W Paton

(Oceans 2000, 1973)

I think there are nine hurdles in the divers' Grand National and, of these, there are two that may or may not prove to be insurmountable obstacles, anaesthesia by inert gases and the effects of pressure per se.

Firstly, to bring out two points about anaesthesia:

Some time ago we at the Medical Research Council did some work on carbon dioxide intoxication: three colleagues and I breathed carbon dioxide at 20 per cent, 15 per cent, 12 1/2 per cent and 10 per cent in oxygen, meanwhile signing our names continuously. Delicate changes in our hand-writing became apparent almost immediately, and finally we reached a stage of total illegibility - at which point we were in fact unconscious, failing to respond to commands, and amnesic.

What I want to point out here is that even though we were unconscious, we were still trying to do the tasks allotted to us, still trying to write. So a person can be quite fundamentally affected and yet still persist in his previous behaviour.

The second point is that even when completely unconscious in these conditions, we were far from being at a state of surgical anaesthesia. There is a great difference between the quantities of narcotic of these anaesthetic drugs that will affect a man's operational efficiency - his judgement, resourcefulness or ability to adhere to a programme - and the amounts necessary to attain surgical anaesthesia.

The reason that most of us believe that anaesthesia is effected by molecules getting into the fatty part of the body is that if you measure the tendency of gases to go into fat, and correlate this with the potency of the gases, you get an extraordinary correlation which deviates from the expected by, perhaps, about 20 per cent, and I think one should rely on this to show that it is a fatty, as opposed to watery, part of the body that is really involved at the molecular level.

Comparison of Rank Order of Inert Gases Low

	Low				**High**
Decompression sickness (1/Poo for mice)	He	N_2	Ar	SF_6	N_20
Water solubility	SF_6	He	N_2	Ar	N_20
Fat solubility	He	N_2	Ar	SF_6	N_20
Total body solubility	He	N_2	Ar	SF_6	N_20

Poo is the maximum pressure from which a rapid decompression to atmospheric pressure is possible without hazard after long exposure.

Comparison of the liability of various gases to produce decompression sickness with their water and fat-solubility, showing the best correlation with fat solubility (or total body solubility, to which fat solubility makes the major contribution with most gases).

The next question is, of course, what do we mean by a fatty part of the body? Membranes are an important class of fatty material. All our cells have a limiting membrane which is a sheet of fatty molecules with a water-attractive head, and

pairs of peripheral tails that dip down like double leaflets. One can envisage the anaesthetic molecule - whether it is chloroform, xenon or nitrogen - getting among these leaflets and disorganising them.

There is another sort of potential hydrophobic or fattiness and that is the lumps - macromolecules - in the membranes, which transport glucose, carry ions and mediate the responses to drugs. Crystallographers have found that these big protein molecules (macromolecules) can coil in a variety of ways so that the water-attractive areas of the molecule and the hydrophobic or fatty components may localise in regions. If this occurs, there is a sort of binding force between the similar fatty materials and it has been suggested that the fatty region may even hold the molecule in position in the membrane. Now, if one inserted an intrusive molecule which has an affinity for fat, it might disorganise the binding which holds the macromolecules.

The next step in our researches both supported this theory and brought us into the field of very high pressures. In our work at Oxford with Brian Smith, Ray Smith and Keith Miller we queried as to whether helium or neon could anaesthetise if pressure were increased sufficiently, and we wanted to be able to compare the effects of pressure applied through a gas (which would dissolve in the body), with pressure applied hydrostatically.

For our experiments we chose the Crested Italian Newt, which is amphibious. The newt, like us, if turned on its back, tends to right itself and if the animal is completely normal it has a hundred per cent response to this rolling reflex.

At pressures of up to 120 - 150 atmospheres, the newt only just began to be affected by neon. A similar experiment with helium produced roughly the same results with the newt 50% affected at about 150 atmospheres. This might have been “anaesthesia”.

Next, we exposed the same animal to water - in which there are no strange gas molecules. This time the newt responded fully at 100 atmospheres pressure but again began to be affected at 120 atmospheres upwards. We concluded, therefore, that if helium and neon are anaesthetics one cannot prove this because the pressure takes effect first.

Then we came to an interesting question: suppose one combined high pressure and anaesthesia, would they add or even mutually potentiate, or mutually antagonise? We began by exposing the newt to about 30 atmospheres of nitrogen; this virtually blotted out its ability to right itself. Then the pressure was further raised using helium, regarding this as equivalent to hydrostatic pressure; the animal presently recovered as the pressure was increased until it practically got back to normal. However, eventually the pressure effect re-established itself and the newt was roughly fifty per cent paralysed, but not as originally, at approximately 150 atmospheres, but at about 250 atmospheres. It looked as though pressure could antagonise anaesthesia, which would support the general theory of the molecule getting into the fatty material, thus impairing its function.

It is known that when anaesthetic dissolves, membranes expand very slightly; at a surgically anaesthetic concentration they expand by about 0.5 per cent. If one estimates thermodynamically how much pressure is needed to neutralise this expansion, one finds that it agrees closely with the pressure we needed to antagonise anaesthesia. Thus, it looks as though expansion is linked to anaesthesia, and if you can prevent the expansion (by pressure) you prevent anaesthesia.

One might think the pressure simply drove the nitrogen molecules out of the membrane; but analysis shows that this effect (which can be calculated) cannot account for it. Instead it appears that in general the entry of inert molecules into the membrane expands it, that anaesthesia occurs when this expansion reaches a certain critical level (estimated as around 0.5%), no doubt because of some disorganization of the structure, and that reversing this expansion by sheer hydrostatic pressure reverses the anaesthesia.

* * * * * * * *

Brief Profile

Professor William DM Paton has been Professor of Pharmacology, University of Oxford since 1959.

After qualifying in medicine in 1942, and undertaking progressively more important radical jobs, his scientific research work began in 1944 when he joined Sir Lindor Brown's team on diving and submarine physiology at the National Institute of Medical Research.

Although later attracted into pharmacology, and distinguishing himself in that field, he has remained associated with high pressure work since then.

* * * * * * * *

PHYSICAL FITNESS EXERCISES

Proposed new unit of measurement:

There are unconfirmed reports that the SUM are shortly to issue details of new Fitness Standards based on the 50 yards sprint measurement unit proposed by the Victorian Minister for Youth, Sport and Recreation, Mr Brian Dixon. He had noted the general lack of interest by the public in improving their health through jogging or cycling, even by the use of stationary cycles. It is his hope that people will be induced to undertake indoor athletics on a regular basis. That the RAN should be in the van of this experiment is only natural.

A $30,000 study has revealed that people can be considered in regard to their attitude to this matter to fall into five groups. Group 1 "the drifters", comprises the 59% who prefer food and listening to records to making the effort. Group 2, about 19%, feel inadequate regarding their athletic performances following failures during their school life. Group 3 was called "the self improvers" and was the 11% who thought their athletic activities were worthwhile as a way of looking good. The fourth Group, about 6%, gave an impression of great activity but talked rather more than they performed. Only 5% were in the "super-tuned young lions" category who are really active and get on with it, finding the inactivity of others surprising.

Mr Dixon, who is a regular morning runner and father of four children, admits to being in the "super-tuned" group. He says that his Department must now take a new approach to physical fitness. "We need to emphasise activity as fun, and just incidentally as useful", he said, adding that he believed that sexual intercourse as physical activity had the fitness value of a 50 yard sprint. "If you are a bedroom athlete there is no reason why your recreational activities can't be enjoyed", he said.

Promulgation of the new tests is eagerly awaited.