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HUMAN PHYSIOLOGY UNDER HIGH PRESSURE

I. EFFECTS OF NITROGEN, CARBON DIOXIDE, AND COLD

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UNTIL recently most work upon human beings under high pressure was concerned rather with the effects of changing pressure than those which occur when the pressure is kept constant. The most obvious effects of compression are pain in the middle ear and often in the sinuses. The latter, however, does not occur in most healthy people, whilst the former can be avoided by training in opening the Eustachian tube. Trained subjects can be very rapidly compressed. Later on the much more serious effects of decompression were noted. These can be avoided by stage decompression (Boycott, Damant & Haldane, 1908), and this in turn can be greatly accelerated if oxygen is breathed instead of air in the latter stages of decompression (Davis, 1935).

Besides effects such as those of cold and of poor air supply which can be readily avoided, two other effects appear at high pressure. One of these is oxygen poisoning. This is particularly dangerous when oxygen is breathed instead of air, as in some types of self-contained diving dress and rescue apparatus. We hope to publish results on this question later.

The second effect, which is now generally ascribed to nitrogen, seems to have been first described by Damant (1930). In his account of a discussion at the meeting of the British Association for the Advancement of Science in that year, he refers to Sir Leonard Hill's description of the mental and emotional abnormalities which occur even in picked divers at such depths as 300 ft. Sometimes such men on their return to the surface had no recollection of events prior to their ascent. High partial pressures of oxygen and impurities in the air were suggested causes of this phenomenon, but Hill's observations on the subject had satisfied him that neither oxygen nor carbon dioxide was responsible.

Phillips (1932) and Hill & Phillips (1932) considered the hypothesis that the behaviour of subjects under high-pressure conditions is to be explained on wholly psychological as distinct from physiological grounds.

Behnke, Thomson & Motley (1935) investigated the effects of air at 3 atm. and over, which they summarized as 'euphoria, retardment of the higher mental processes, and impaired neuro-muscular co-ordination', and they put forward for the first time the considered opinion that the operative factor was nitrogen (without excluding the rare inert gases). They believed that nitrogen acts on the nervous system by virtue of its high solubility coefficient in lipoid substances as compared with that in water. They recorded, however, the fact that the symptoms are immediate in their onset. It is noteworthy, incidentally, that the symptoms described by these workers seem decidedly more profound in degree than those which we observed, of which an account is to be given. For example, in the (apparently) sole test which they carried out at 10 atm., stupefaction was recorded and the palpation of a person's pulse was stated to be a task attended by great subjective difficulty. The desirability of the use of an artificial gas mixture for divers and caisson workers was stressed, and it was suggested that nitrogen should be replaced by a rapidly diffusible, sparingly soluble gas with a low partition coefficient for lipoid/water systems. Helium was not specified, but was in fact the gas in contemplation. At that time its very high cost was an obstacle in the path of its adoption.

The proposal that helium might advantageously be substituted for nitrogen in gas mixtures for high-pressure work had already been made some years before. It seems to have originated with Elihu Thomson in 1919 and 1920, a fact to which attention was drawn by the worker in question in 1927.

Hildebrand, Sayers & Yant (1928) discussed the subject and remarked that as early as 1919 a patent had been applied for (by C. J. Cooke, of Washington, D.C.) regarding the use of helium-oxygen mixtures for workers under pressure.

It is important to realize that these and similar suggestions for the use of helium were made purely from the standpoint of shortening the time necessary for decompression without simultaneously increasing the liability to 'compressed air illness' in its various manifestations, which was known to be attributable to atmospheric nitrogen. It was not until attention had been drawn to the psychological results of working in compressed atmospheres, as in the communication of Damant cited above, and until the work of Behnke and his colleagues had made it likely that nitrogen was responsible for these effects, that helium began to be studied from the point of view with which we are mainly concerned in this paper. Now, in the opinion of Behnke & Yarborough (1938), the position is that 'the improved mental condition of the diver has supplanted the saving in decompression time as the most important expected advantage in using helium'.

Shilling & Willgrube (1937) studied mental and neuro-muscular reactions in compressed air in a quantitative way. Like all the American workers, they emphasize the 'stimulation and well-being' experienced by subjects at five or more atmospheres. They imposed a set of tests not uncomparable with, but perhaps rather more exacting than the ones we have used, and they observed deterioration in performance under pressure, with experienced as well as inexperienced subjects. In discussing the aetiology of the effects, they remark upon the facts that the greatest change is noticeable immediately on reaching the pressure, and that if a man is compressed too quickly he becomes unusually dizzy and dazed and requires some minutes to attain comparative normality. At present, as we ourselves agree, the nitrogen narcosis theory does not seem to offer a complete explanation of such facts.

End (1937), in a series of experiments primarily concerned with the shortening of decompression times by the use of helium-oxygen mixtures, was also led to the conclusion that helium could be instrumental in freeing divers from the untoward psychological effects of air at high pressures.

The same author (1938) describes a world record dive (in 420 ft. of fresh water) made by Nohl in a suit of special design, breathing a helium-oxygen mixture. It is stated that mental symptoms were entirely obviated, though in view of the fact that the diver was a man of calm temperament and unusual intelligence, no sweeping conclusions are drawn.

Behnke & Yarbrough (1938), in a comprehensive study of helium from a physiological aspect, made a number of observations that are of interest in view of our findings, to be reported in this paper. The most striking bodily effect, they say, is the feeling of normality in contrast with the usual intoxication and sense of pressure and depth associated with high air pressures. At a pressure corresponding to 500 ft. of water, the subject felt well, and it appeared to him that he was at a depth of not more than 100 ft. At 300 ft., when air was suddenly supplied to a diver breathing helium, dizziness and loss of muscular control were produced, together with a sensation of 'floating away'.

Behnke & Willmon (1939) observed mental disturbance in divers working at 240 ft. in the salvage of U.S.S. *Squalus*. The authors were surprised at the unusual intensity of the symptoms that occurred, and their communication is of interest because they found an accumulation of carbon dioxide in the divers' helmets. The symptoms, nevertheless, were not typical of high carbon dioxide concentration in the lungs, but rather of air at pressures higher than actually obtained. Their conclusion was that the increase in carbon dioxide tension augmented the narcotic action of the nitrogen; and it is stated in support of this that such symptoms can be decreased by lowering the carbon dioxide by excessive ventilation. The troublesome symptoms in this series of operations were overcome by the substitution of helium-oxygen mixtures for air.

It was the object of the experiments here recorded to confirm the work of the American investigators on nitrogen narcosis, and also to investigate the concomitant effects of carbon dioxide and cold. For at 10 atm. pressure a carbon dioxide concentration of 0·5% gives a partial pressure of 5%, which may be expected to have some physiological effect. And the sea water at a depth of 300 ft. is often much colder than the surface water. For these reasons Admiral Sir M. E. Dunbar-Nasmith's physiological subcommittee for saving life from sunken submarines asked us to furnish information on the subjects discussed in this paper, and some others, while Messrs Siebe Gorman and Co. were so kind as to place their equipment and the services of their staff at our disposal.

Methods and personnel

All the experiments were conducted in a cylindrical steel chamber of 100 cu. ft. capacity. Its horizontal length is 8 ft., its diameter 4 ft. Thus two subjects can use it at a time. The experiments were done on E. M. C. and

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J. B. S. H. together, or on another subject, with one of them acting as an observer. The only experiment in which one of us went in with two others was unsatisfactory, as one of the subjects became obstreperous, and interfered with tests carried out by the other. Lighting is through windows from the outside. There is no telephone, but communication took place by a code of taps, by messages shown at the windows, and by shouting. The pressure was raised by air from cylinders outside. CO_2 was added from cylinders of liquid CO_2 inside, besides what was produced by the subjects. Air samples were taken in the chamber, and analysed later with the Haldane apparatus at atmospheric pressure. Owing to the small size of this chamber, subjects could not stand, and it is conceivable that this may explain some of the differences between our results and those of the American observers.

Decompression was carried out in accordance with the tables published in Davis's *Deep Diving* (1935). It was facilitated by breathing O_2 at pressures of 3 atm. and less. In this way the time needed for decompression after 16 min. stay at 300 ft. of salt-water pressure (10 atm.) is reduced to only 59 min. Our only deviation from the tables, except where the contrary is stated, consisted in the fact that we added half the period of compression, instead of the whole of it, as recommended, to the time spent 'at the bottom'. The O_2 used in the later stages was supplied from cylinders in the chamber, and breathed from the 'Salvus' apparatus in which the CO_2 expired is absorbed by soda-lime.

As a test of manual skill we used the R.-V. Manual Dexterity Test, supplied by the National Institute of Industrial Psychology. A number of steel ball bearings must be placed in three holes. During a first period of 1 min. they are picked up with a forceps and placed in the first hole, during a second minute they are placed in the second hole with a scoop, and during the third in the third hole with finger and thumb. The subjects were always given a preliminary test before their first recorded test in the chamber at atmospheric pressure. A typical score was $21+14+25=60$, the second minute's work being almost always the most difficult. The scores varied considerably both between individuals and with lighting, seating, and other arrangements; but we were only concerned with the differences produced by the pressure change.

As a test of intellectual ability we gave a series of four-figure multiplications, e.g. 9746×4956. Rapid calculators could do ten such in 6–8 min. Others were required to do five to eight only. The time taken and the number correct were recorded. The subjects were also encouraged to take notes, and these latter afforded valuable evidence of their mental condition and muscular co-ordination.

In experiments where CO_2 was added, E. M. C. or J. B. S. H. often breathed through a canister containing soda-lime, whilst observing the other subject. However, owing to the intoxicating effect of the N_2, this precaution was sometimes omitted, and for the same reason the observations were sometimes imperfect. An external observer watched through a small window, but could only note the more striking symptoms of those within.

The following subjects were used. The age is given in each case. Jermyn and Spurway are females:

W. Allen, 30.	J. Larmour, 30.
S. Callaway, 24.	B. Matthews, 36.
E. M. Case, 35.	J. Millie, 34.
O. Daniel, 23.	J. Negrin, 48.
J. B. S. Haldane, 47.	J. Prendergast, 26.
T. S. Hardie, 31.	J. M. Rendel, 25.
J. E. Jermyn, 24.	H. Spurway, 25.
H. Kahle, 41.	R. Winfield, 30.
H. Kalmus, 34.	

The majority are English, but two are Irish, one Spanish, one Czech, and one German. Their occupations had varied from prime minister to tailor, and loader for a transport company. The majority are, however, university graduates.

Mechanical effects of compression and decompression

Though our main object was not to study the effects of compression and decompression, our observations thereon are not without interest. During compression all subjects noticed slight pain in the ears, and a few of them in sinuses. We were, however, surprised at the ease with which most of them could be compressed, even at the first trial, after being told how to force air into the Eustachian tubes by holding the nose and blowing. Unless suffering from a cold, it was exceptional for a subject, even at the first attempt, to require as long as 6 min. for compression to 10 atm.

In view of a suggestion that men without biological training might find difficulty in inflating their Eustachian tubes, we paid special attention to four working-class subjects. Each was shown how to compensate for rising pressure by holding his nose and blowing, and allowed to stop the compression if he felt pain. The longest time taken to reach 10 atm. was 5 min.

Our three most difficult subjects were B. M., J. N., and H. Ke. B. M. had a fairly severe cold, and, although he used a benzedrine inhaler, took $9\frac{1}{2}$ min. to reach 10 atm. J. N. had trouble with his left ear, and several stoppages were necessary before 10 lb. pressure (1·7 atm.) was reached. Then some obstruction appeared to give way, and a pressure of 10 atm. was reached in 11 min. H. Ke. had had both eardrums burst by shell fire in 1917, and in his first experiment it took 26 min. to compress him to 8·6 atm. He was later given several educational compressions to 2 atm., and found that swallowing was more effective than nose-blowing in opening his Eustachian tubes. At the time of writing he still requires about 10 min. for compression to 6 atm., but seems to be improving rapidly.

We think that the vast majority of subjects could be trained to adjust rapidly, but it is important that instructions should be given tactfully and that the subjects should have full confidence. We and our trained subjects can be compressed to 10 atm. in $2\frac{3}{4}$ min., and were apparatus available, could certainly be compressed much quicker. Even with a severe cold E. M. C. had no difficulties during compression, but had sinus and ear pains during decompression.

The quickest compression recorded is from 1 to 7 atm. in 90 sec. This caused no after-effects, and no appreciable discomfort. It corresponds to a descent of 133 ft. per min. in sea water, which is near the record for a diver. The absolute rate of pressure increase, of $\frac{1}{2}$ atm. in $7\frac{1}{2}$ sec., corresponds with that which would be experienced by the pilot of an aeroplane diving vertically from some 18,000 ft. to ground-level in $7\frac{1}{2}$ sec., that is to say at over 1600 miles/hr. Clearly therefore trained and picked pilots are not likely to suffer from this cause for many years to come.

We had one serious casualty. J. M. R. was thrice compressed to 8·6 atm. (250 ft.) in the course of a month. One or two hours after the first experiment he noticed a pain referred to the left axilla which he attributed to 'indigestion' following a meal. The second experiment had no such effect. The third caused a return of the pain, and shortness of breath. These symptoms persisted, and 16 days later he was examined by Dr A. Morland, of University College Hospital. He found 'signs of pneumothorax on the left side, the heart being displaced about $1\frac{1}{2}$ in. to the right. X-ray examination confirmed the presence of the left-sided pneumothorax. It also showed three thin-walled cavities having the appearance of emphysematous bullae at the extreme right apex. There was no evidence of tuberculosis.'

He was admitted to hospital, and found to be free from symptoms except those directly due to the pneumothorax. Twenty-three days after the last experiment Prof. R. S. Pilcher carried out a thoracoscopy at Leavesden Hospital under local anaesthesia. He reported as follows:

'The left lung was found to be nearly fully collapsed. No bullae were seen on the surface nor any stumps of adhesions. The apex of the upper lobe had a curious notch in the upper border of the lobe. This notch was whitish in colour, and in a groove running along it was what looked like a small blood clot. On the lung below the notch was a narrow band of fibrin. This appearance may have been due to a ruptured bulla, but no others were seen. The patient inhaled cigarette smoke during the examination, but no escape into the pleura was seen. There was no blood or fluid in the pleura.'

The patient made a slow but uneventful recovery. Five months after the first experiment there was a slight relapse. J. M. R. felt bubbles in the right side, but no pain. An X-ray examination showed a small bubble of air in the pleural cavity, which disappeared spontaneously. Eight months after the first experiment there was a more serious relapse. The left lung collapsed completely. Prof. Pilcher performed a thoracoscopy and found that an adhesion had given way. He then blew in fine-grained talcum powder, producing a sterile inflammation which caused the lung to adhere to the pleura. It is hoped that this will prevent any further relapse.

Dr Morland has little doubt that J. M. R. suffered from a rare congenital condition, in which weak areas are present in the lungs. J. M. R. was an athlete, and had had numerous routine examinations of the lungs, but no X-ray examination with special reference to this condition.

The immediate cause of the rupture is not clear. Any of the following would seem to be possible:

(*a*) The lung was over-distended while inflating the Eustachian tubes during compression.

(*b*) The subject held his breath during a decompression, and the expansion of the air brought about the rupture.

(*c*) During one of the later stages one of us turned on the by-pass of the 'Salvus' apparatus too rapidly and fully, thus causing a sudden increase in the gas pressure in the lung. One of us has himself experienced a definite though transitory pain from this cause.

(*d*) A bulla with poor communication with the bronchi existed and filled up with air at high pressure. During decompression the air could not escape into the bronchi, and burst out into the pleura. However, the communication with the bronchi was sufficient to allow leakage.

In the absence of further information we cannot distinguish between these hypotheses.

Before we were convinced of the validity of the nitrogen narcosis theory we made some observations on the circulation. They are somewhat incomplete, and since they are probably in part due to the effects of high-pressure O_2 they will be discussed in a later communication. It is sufficient to state that there were no changes either in pulse rate or systolic pressure which could possibly account for the symptoms described later. Both rate and pressure rose in some cases and fell in others, the changes in subjective feelings and behaviour being nevertheless much the same in the two cases.

Besides this, E. M. C., J. B. S. H. and H. Ke. had fillings in teeth loosened, and J. B. S. H. lost a dead tooth which had been quiescent since 1906, but began to hurt during decompression, and developed an abscess. Such effects are well known both in divers and aeroplane personnel.

The usual effects of pressure on the voice were noticed. When E. M. C. was compressed to 10 atm. during an attack of laryngitis, he found speech much easier at pressures above 4 atm. The effect of H_2 and the similar effect of He on the timbre of the voice persisted at 10 atm., though less striking than at atmospheric pressure. At 320 ft. (10·7 atm.) a cylindrical flageolet ('tin whistle') required greatly increased effort to blow it. The pitch was unaltered, but the tone was fuller and rounder than normal, rather like that of a recorder, and the second octave was difficult to execute clearly. The pitch of an oboe reed was much reduced, and a tuning-fork gave its normal note. At high pressures loud cracking noises, audible to others, were frequently produced when J. B. S. H. moved his shoulder joints. Clearly the pressure between the articular surfaces is increased tenfold, and the effect of irregularities must be enhanced. No pain was associated with these sounds. J. N. noticed 'strange sensations on the lips, something like velvet'. J. B. S. H. noticed them on several occasions subsequently. We have no explanation to offer.

A point of some practical importance was noted in connexion with breathing apparatus. Whilst observing the reactions of others in mixtures containing much CO_2 under high pressure, E. M. C. and J. B. S. H. were provided with mouthpieces attached to canisters containing soda-lime, to remove CO_2 from the inspired air. The resistance of these became very large. For the volume breathed per minute remains approximately constant when the pressure is raised, whilst the mass per minute is proportional to the pressure. Thus, if other things are equal, the work done per minute in breathing is ten times as great at 10 atm. as at 1 atm. But other things are not always equal. At high pressures, flow through an orifice becomes turbulent at velocities which do not give turbulence at a lower pressure. If so, resistance rises a good deal more than ten times.

Not only did the resistance of certain canisters become unbearable, but they gave off caustic dust which caused coughing, though they had not done so at atmospheric pressure. This is explicable if turbulence set in. As a result of this resistance, coughing, and particularly the lack of self-control caused by N_2, both of us, but particularly J. B. S. H., tended to remove our respirators, or not to put them on after speaking to other subjects. Our observations were often faulty, and we sometimes lost consciousness when this was not intended.

It is very desirable that all breathing apparatus intended for use at high pressure should be tested at that pressure. We wish, however, to state that in the Davis Submarine Escape Apparatus tested by us there was no unpleasant resistance even at 10·7 atm. (320 ft.).

Effects of decompression

When we adhered to Davis's tables the symptoms noted were generally slight. Most subjects complained during decompression on one occasion or another of itching, often accompanied by a slight rash. Both itching and rash disappeared after an hour or so at atmospheric pressure. Three subjects had nose bleeding during decompression. In one it was repeated. In the other two it only occurred once in a series of experiments.

It is possible that the rash and the nose bleeding are related, both being due to extreme dilation of the skin vessels. They can hardly be due to numerous small air embolisms, or they would be accompanied by more serious symptoms. They may possibly be due to impulses from posterior roots, similar to those causing 'bends' which are at least partly of central origin. However, we are not prepared to offer any definite explanation.

When the tables were adhered to, only four subjects out of fifteen, namely, T. S. H., J. E. J., H. Ke. and H. S., had bends. The pain was localized in the arms or more rarely in the legs, and was fairly severe in T. S. H. and H. S., sometimes lasting till the next day. H. Ke. is fairly fat, but not so fat as J. N. and J. B. S. H. J. E. J. and H. S. have the subcutaneous fat normal to their sex, but no more, whilst T. S. H. is definitely thin. So there is no obvious correlation with fatness.

When the tables were not adhered to, bends were more frequent. Thus J. B. S. H. and H. Ke. took 26 min. to compress to 8·6 atm. (250 ft.). They remained for 32 min., and were decompressed according to a schedule calculated for 45 min. stay at 250 ft. Both developed bends, H. Ke. rather severely, but J. B. S. H. slightly. J. B. S. H. also developed slight bends after an experiment at 8·6 atm. 3 days later in which the time table was adhered to. He did not develop them in any of over thirty later experiments at 8·6 atm. and above.

Subjects B. M. and R. W., who are attached to the Royal Air Force and wished to experience bends, were compressed to 10 atm. in 9½ min., and after remaining at this pressure for 7½ min. were decompressed in accordance with the time table for 12 min. at 300 ft., which assumes oxygen breathing from the 60 ft. stage to surface. However, neither breathed it, though J. B. S. H. who was with them, supervising the experiment, did so. B. M. developed pains in the buttocks and neck, and had somewhat impaired vision during the latter part of the decompression. On emerging, the pain became worse, and spread to the shoulders. R. W. had no symptoms other than itching and fatigue. B. M.'s symptoms disappeared after about 2 hr.

E. M. C. has on several occasions breathed air instead of O_2 during one to three stages of the decompression, without experiencing bends or other untoward symptoms. On three occasions he has breathed air throughout while being decompressed in accordance with the O_2-breathing schedules. The first of these was after 8 min. at 10 atm., for 4 min. of which period he had been breathing a H_2-O_2 mixture. There were no symptoms. The second was after 10 min. at 7 atm. in air, and slight bends in one elbow and wrist resulted, lasting for a few hours. The third occasion was a decompression (from 20 min. at 10 atm.) during which air had been breathed. The decompression lasted for 86 min. Distinct but not severe pains in both hips and shoulders developed immediately on emerging, and lasted for some 48 hr., together with a slight general feeling of malaise.

It is clear that individuals vary greatly in their susceptibility, and probably somewhat from day to day. The schedule is not quite satisfactory for some persons, notably H. S. and T. S. H. It could be greatly shortened for E. M. C. and R. W. Indeed, for the latter the time could probably be halved. It is very possible that even the susceptible persons would have escaped, had they taken vigorous exercise during decompression, as recommended. This is difficult in the small chamber used.

As related later, a mixture of 85% He and 15% O_2 was breathed on several occasions by E. M. C. and J. B. S. H. After breathing this for 11 min. at 10 atm. in a self-contained apparatus, O_2 being added from a cylinder and CO_2 absorbed by soda-lime, J. B. S. H. was decompressed according to the usual schedule. He noticed no itching during decompression. But on emerging there was severe pain in the right hip and both shoulders, becoming worse on moving; and itching of the back. An hour later there was also severe pain in the buttocks, and a burning pain in the skin of the left scrotum and thighs, later spreading to the calves.

Next day there was itching over a nearly symmetrical area reaching in the sagittal plane from the back of the scrotum to near the base of the coccyx, and laterally as far as the ischial tuberosities, rather farther on the right. He was constipated for 3 days, and then had burning pain on wiping the anal mucosa. These symptoms persisted for 3 weeks, and then abated, but after 6 months there was still itching and some anaesthesia over the coccyx. The original distribution of the itch corresponds to that of the 4th and 5th sacral roots, the distribution after 6 months to that of the 5th sacral roots. Dr E. A. Carmichael suggests that the lesion, presumably caused by a bubble, is located near the tip of the conus.

E. M. C. repeated the experiment, breathing the He-O_2 mixture for 19½ min. including the first 9 of decompression, and then changing to O_2. He had no symptoms. J. B. S. H. therefore breathed the mixture at 10 atm. for 9 min., and for the first 6 min. of decompression. To his relief he had no symptoms beyond a faint itch on the forearm.

The result is therefore inconclusive. All that can be said is that out of some forty decompressions from 8·6 or 10 atm. the only occasion on which J. B. S. H. had serious bends, when adhering to the schedule, was after breathing a mixture where He was substituted for N_2. It is difficult to suppose that this was quite fortuitous. And it is certain that a mixture of this kind cannot be regarded as superior to air as a prophylactic against bends, as has been claimed by some, but not all, American workers.

In a number of experiments, as related below, CO_2 was added to the air breathed at 10 atm. This caused hyperpnoea, and probably vasodilation. During decompression the partial pressure of CO_2 fell, so that there was no hyperpnoea and presumably no vasodilation. We expected that in consequence more N_2 than usual would be absorbed at the high pressure, and no more given out during decompression, and hence that bends would occur. However, no one developed bends under these conditions except H. S. and J. E. J. The former had had them without CO_2, and did not develop them after breathing the largest concentration of CO_2, which made her unconscious. The latter has not been tested without CO_2. It appears, therefore, that CO_2 does not appreciably increase the incidence of bends.

Our longest stay at 10 atm. pressure was 30 min. We were compressed in 4 min., and the decompression took 2 hr. 39 min.; during the last 2 hr. and

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10 min. we breathed O_2. In general we did not stay for more than 12 min. at this pressure, decompression lasting for an hour.

NITROGEN INTOXICATION

Only ten subjects were subjected to high pressure without the addition of carbon dioxide. However, it will be seen that many of the effects observed when carbon dioxide is added are N_2 effects.

E. M. C. and J. B. S. H. can barely notice anything abnormal at 5 atm. (130 ft.). At 6 atm. there is a slight but definite change in the consciousness, which is marked at 8·6 atm. (250 ft.) and very strong at 10 atm. (300 ft.) Most of the experiments were done at these two latter pressures. At 6·3 atm. (177 ft.), in a single experiment the total score in the skill test fell from 143 to 140. The mean time of the arithmetic test fell from 8 min. 11 sec. to 6 min. 51 sec., and the mistakes from 6 out of 20 to 3 out of 20. Thus there was no evidence whatever of deterioration. In view of the results of American workers, it is, of course, possible that others might have been more affected; however, E. M. C., J. B. S. H. and H. Ke. are pretty normal at 7 atm.

Seven subjects were tested at 8·6 atm. (250 ft.). E. M. C. and J. B. S. H. were slightly confused. Two others were distressed, and felt as if they were going to faint. One was euphoric and talkative, feeling very confident, another mildly elated. The fifth was perhaps unusually obstinate, but showed no obvious emotional reaction. The mean score of five subjects in the manual dexterity test was 64·8 at atmospheric pressure, 66·0 at 8·3 atm. The difference is insignificant. In two subjects a further test after 24 min. under pressure showed no deterioration.

The results of the arithmetic tests were very different. The time taken was generally, but not always, increased. In four subjects the number of mistakes increased from six to twenty-two in a total of thirty-three sums. One subject (H. S.) was exceptional in making only one mistake out of six in each series, though under pressure she had to do her arithmetic aloud.

Five subjects were tested at 10 atm. (300 ft.). The results on eleven subjects at 10 atm. pressure with additional CO_2 are reported later. E. M. C. and J. B. S. H. were somewhat euphoric on the first occasion, but later on this wore off; however, both, and especially J. B. S. H., always tended to make notes which were intended to be humorous, and were sometimes improper. They were always rather confused. J. N. preserved complete outward calm. R. W. laughed a good deal, and 'cheated' in the dexterity test. B. M. varied between depression and elation, at one moment asking to be decompressed, because he felt 'b... awful', and the next laughing, and attempting to interfere with R. W.'s dexterity test. E. M. C. and J. B. S. H. had a mean score of 79·2 at atmospheric pressure and 72·4 at 10 atm. in a total of five experiments. Before one pair of these they had taken 15 and 10 mg. benzedrine respectively. Their scores after this were higher throughout, but fell slightly under pressure. $t = 3{\cdot}16$ for 4 degrees of freedom. The probability that this is due to chance is about 0·04. But J. N.'s score rose from 54 at 1 atm. to 55 at 10 atm. R. W. also increased his score from 57 to 60, but was detected 'cheating', i.e. picking up two balls at a time, although he is a responsible scientist at atmospheric pressure.

The arithmetic was probably worse than at 8·6 atm. E. M. C. made ten mistakes out of twenty, J. B. S. H. nineteen out of twenty-one, as compared with normal values of three and five mistakes out of twenty, respectively. B. M. completed one sum in 12 min. This was wrong.

Perhaps of even greater importance are the observations made on our practical activity and judgement. J. B. S. H. was more affected than E. M. C., but both found it hard to carry out several different tasks; for example, timing a test on another subject, taking notes, and taking gas samples. For this reason several arithmetic tests were not timed, and other observations were not as satisfactory as could have been wished. Thus J. B. S. H. noted down a failure to press the button of the stopwatch as 'forgot to turn tap'. It is quite imperative that no great trust should be placed in human intelligence under these circumstances. For example, J. B. S. H. poisoned himself with O_2 and had severe convulsions through a mistake which would have been unpardonable at atmospheric pressure. Handwriting generally deteriorated.

In a single experiment at 10·7 atm. (320 ft.) E. M. C. and J. B. S. H. felt no worse than usual, and were able to make observations. It is quite incorrect to say that people are stupefied at such pressures, as will come out even more forcibly when the effects of adding CO_2 are considered. However, they are definitely less responsible than when normal.

Subjectively many subjects reported that they felt drunk. J. B. S. H. felt somewhat mystical. His consciousness was invaded by words, sometimes nonsensical and always irrelevant, which appeared to him to be very important at the time, and by memories of childhood. H. S. not only felt all sensations as abnormal, but had a strong conviction of sin, and of the necessity of divine grace. The subjective symptoms were already beginning when 'bottom' was reached, were maximal within 2 min., and no worse after 30 min. at 10 atm. We have the impression that there is a slight degree of habituation. However, we have no objective evidence for this. And if it exists it may be purely psychological. On a first compression the change of consciousness is very striking, and alarms some people. When it is taken for granted, it is likely to have less effect on behaviour.

On decompression there was almost always an immediate feeling of subjective improvement when the pressure was reduced to 5 atm. 'I feel normal again', 'Erholt sich alles', and 'My god, I'm sober', are typical notes. The handwriting and arithmetical ability improved. It is clear that the main effect of the high pressure was on the higher functions of the brain, intellectual and moral performance being much more affected than muscular skill.

A canary was not merely able to stand on its perch, but to fly round the chamber, and alight satisfactorily. This is of interest, since the increased density of the air was obvious to human observers moving their hands. On the other hand, *Drosophila melanogaster*, a small fly, walked but would not fly, even when mechanically stimulated.

Our experiences with mixtures containing He and H_2 leave us in no doubt that our symptoms were due to N_2. It is, however, possible that this gas may act by interfering with oxidation in the tissues. If this interference occurs at an early stage, there should be antagonism between N_2 and O_2, and the symptoms at a given partial pressure of N_2 should be worse if that of O_2 is lowered. In air at 10 atm. the partial pressure of O_2 is 2·1 atm. A mixture of 98% 'nitrogen' (atmospheric) and 2·3% O_2 was therefore stored under pressure, and breathed through non-return valves. At atmospheric pressure it naturally caused asphyxia in both of us. At 8·6 atm. this mixture had a partial pressure of 8·4 atm. N_2, as compared with 7·9 in air at 10 atm., and 20% of an atmosphere of O_2, as in air at a pressure of 0·94 atm. J. B. S. H. breathed it for 17 min., and retained consciousness, but made five out of five arithmetical mistakes. E. M. C. breathed it for the last 7½ min., but felt no change of consciousness on doing so. However, as he attempted to blot his pencilled notes, he was by no means normal. In another similar experiment the mixture contained only 1·5% O_2, so that the partial pressure of O_2 was 12·9%. J. B. S. H. breathed this for 6 min., and E. M. C. for 8 min. Both had hyperpnoea, and felt worse than in ordinary air, the former feeling much better on breathing air at 8·6 atm. Neither lost consciousness, and J. B. S. H.'s score on the dexterity test was only reduced from 70 to 53. It is, we think, clear that there is little synergism between N_2 excess and O_2 shortage.

The following incidental observation was made. J. B. S. H. usually and E. M. C. once or twice noted a peculiar taste. A number of other subjects did the same, and one noticed a smell. The taste was variously described as metallic, harsh, salty, and indefinable. It was noted when the O_2 pressure had not been raised. Moreover, at 3 atm. pressure O_2 has no taste, though J. B. S. H. constantly, E. M. C. once, and H. Ks. on the only occasion when he was tested, have noted an astringent and slightly sweet taste confined to the back or the lower surface of the tongue when breathing it at 5 or 6 atm. Thus the harsh or metallic taste is probably that of N_2.

EFFECTS OF BREATHING MIXTURES WHERE HELIUM OR HYDROGEN IS SUBSTITUTED FOR NITROGEN

A mixture containing 85% He and 15% O_2 was prepared and compressed in a cylinder. This was let into a Douglas bag, and rebreathed through a canister absorbing CO_2. It was renewed from time to time to avoid O_2 want. E. M. C. first breathed O_2 for 12 min. at atmospheric pressure to get rid of N_2, then washed his lungs out repeatedly with the He-O_2 mixture, and was compressed to 10 atm. He felt no trace of discomfort apart from heat due to adiabatic compression. He made one mistake out of ten sums, but noticed a twitching of the lips, which passed off, and was not noted in later experiments. After 10 min. at 10 atm. he began to breathe air. His voice was thin and nasal. There was no instant subjective effect, but after 2 min. he felt 'slightly cock-eyed', and after 3 min. had the full subjective symptoms. J. B. S. H. did not start breathing the mixture till 10 atm. pressure was reached. He felt a great relief of his symptoms, and his arithmetical performance was normal. After $5\frac{1}{2}$ min. he started breathing air. There was a slight feeling of giddiness after $1\frac{1}{4}$ min. and a marked change of consciousness after 2 min.

In two later experiments on J. B. S. H. and one on E. M. C., the same mixture was used, but it was placed in the bag of a Davis Submarine Escape Apparatus and rebreathed, O_2 being added at a rate of 130 c.c. per min. from time to time. J. B. S. H. began breathing the mixture at atmospheric pressure. At 10 atm. he felt slightly abnormal for a short time, perhaps because he had got rather short of O_2, preferring the risk of asphyxia to that of convulsions. He could, however, do mental arithmetic such as 97×43 correctly after 8 min. After this experiment he had the nervous symptoms described above. In a similar experiment E. M. C. began breathing the mixture on reaching 'bottom' (10 atm.) and noted a subjective change for the better in 1 min. Another experiment on J. B. S. H. designed to test decompression effects produced a similar result.

We next proceeded to substitute H_2 for N_2. A mixture of 4 vol. of H_2 with 1 vol. of O_2 is highly explosive, so that its physiological properties would only be of theoretical interest. However, according to information kindly given to us by Prof. A. C. G. Egerton, Secretary of the Royal Society, H_2-O_2 mixtures do not explode at 10 atm. if they contain over 96% of H_2, nor H_2-air mixtures if they contain over 68·7% of H_2. A mixture of one part of air with nine of H_2 is therefore entirely safe, and yet, at 10 atm., it contains as much O_2 in a given volume as the same amount of air at atmospheric pressure. We filled two Douglas bags with air at atmospheric pressure, and added H_2 from a cylinder during and after compression to 10 atm., mixing the contents thoroughly. We then breathed the mixture through non-return valves. J. B. S. H. breathed it for 6 min., E. M. C. for about 4 min. J. B. S. H. made one mistake in four sums, perhaps because the gas rising in front of his eyes made writing difficult. Both felt normal, but found the mixture unpleasantly cold. We are not in a position to compare the physiological effects of He and H_2. To do so it would be necessary to carry out experiments at 20 or 30 atm., where one or both of them may begin to have an effect.

Behnke & Yarbrough (1939) report that the narcotic effect of A is somewhat greater than that of N_2. A single experiment on E. M. C. in which A was substituted for the N_2 in air at 6 atm. led to a deterioration in the manual dexterity test, but no noticeable subjective changes. Nor did bends develop on decompression according to the usual schedule. Thus our observation, so far as it goes, confirms Behnke & Yarborough.

These experiments leave no doubt in our minds that Behnke *et al.* (1935)

were entirely correct in ascribing the effects of compressed air on consciousness and behaviour to its N_2 content, even though we differ from them slightly as to the effects found. But it is far from clear to us which are the relevant properties of the gases in question. Our experience with resistant canisters rules out the possibility that the good effect of He when replacing N_2 under pressure can be due to diminished respiratory resistance, which probably accounts for its good effect on asthma. On changing from one gas to another, the subjective change takes several minutes to develop. Hence they cannot be due to the physical properties of the gases in the gas phase. Nor can they be due to their rates of diffusion when dissolved, as the symptoms due to N_2 reach their maximum after about 3 min. The differences between different gases must, we think, be due to their activity or inactivity in the brain tissue itself. The following solubilities at 38° C. are taken from Behnke & Yarbrough, and from Seidell's (1940) tables:

Gas	H_2O	Olive oil	Benzene
H_2	0·0165	—	0·076
He	0·00872	0·0148	0·021
N_2	0·01275	0·0667	0·116
A	0·0262	0·1345	0·222

It is at once clear that solubility in water cannot be the decisive property, for H_2 is more soluble than N_2. The data on solubilities in oils are not quite comparable, but the following facts are to be noted. The solubility of H_2 in cotton-seed oil and train oil is about 0·04 at 100° C. and 0·055 at 180° C. Thus at 38° C. it is probably about 0·03 (Ubbelohde & Svanoe, 1919). The solubilities in human fats are probably of similar magnitudes, and that of N_2 not more than double that of H_2. The solubilities of these gases in heavy naphtha and gas oil (hydrocarbon mixtures) have been directly compared, that of N_2 being about 0·10, of H_2 0·07. If the solubilities in fat were in the same ratio, and the narcotic effects proportional to them, the effect of 9·8 atm. of H_2 would be the same as those of 8·7 atm. of air, which is certainly not the case. Even if the solubility of H_2 were only half that of N_2, we should expect the same degree of narcosis as in air at 6·2 atm. We are inclined to doubt whether this is so, though the effects which we observed at this pressure of air were very slight. On the whole, then, our results do not favour the theory that the narcotic effect of 'indifferent' gases is proportional to their lipoid solubility.

We clearly cannot ascribe the narcotic effect of N_2 to chemical properties, since A has none. But other physical properties are very different in H_2 and He on the one hand, and N_2 and A on the other. Thus Armstrong (1908) found that a particular charcoal at 0° C. adsorbed 4 vol. of H_2, 2 vol. of He, 15 vol. of N_2, and 12 vol. of A. It is at least possible that adsorption on surfaces within or on the cell may be as important as lipoid solubility in determining the narcotic properties of gases.

Carbon dioxide at atmospheric pressure

Several observations were incidentally made on the effect of CO_2 at atmospheric pressure. They are given here for comparison with its effects under pressure. In five experiments on various subjects the mean skill test score without CO_2 was 81·4, in 3–4% CO_2, 82·4. The mean percentage of arithmetical mistakes fell from 32 to 24. Neither change is significant, but clearly this amount of CO_2 has no bad effect, though it causes quite noticeable hyperpnoea. With about 6% of CO_2 J. B. S. H. and E. M. C. also found a slight but insignificant improvement in their performance at both tests.

These tests were made after a few minutes' exposure to the CO_2. However, there is little cumulative effect of CO_2 after several hours. Thus in another experiment where the partial pressure of CO_2 was gradually rising from 5·2% at 9 a.m. to 6·8% at 12.40 p.m., J. B. S. H. was able to do CO_2 analyses up to the end, the results checking with one another and the arithmetic being correct, although there was violent panting throughout this period, and some headache, photophobia, and nausea towards the end. The total pressure on this occasion was 1·1 atm. On other occasions this subject has carried out gas analyses in 7½% CO_2.

Thus CO_2 at 6–7% causes relatively little mental impairment or deterioration of manual skill, though most, if not all, people find it distressing. There is, of course, a slight degree of impairment of both manual and mental work, but the latter at least is far less than that produced by air at 10 atm. pressure.

Combined effects of carbon dioxide and pressure

This has been tested on eleven subjects, some of them on a number of occasions. In all but two cases the pressure was 300 ft. (10 atm.). The procedure varied. In a few cases CO_2 was not added till after the high pressure had been reached. In most experiments some at least was added before or during the compression, so as to ensure thorough mixing, whilst more was often added afterwards, the subjects stirring the air to the best of their ability. Analyses seemed to show that mixture had generally been pretty complete.

Breathing increased noticeably whenever the partial pressure rose above 3%, that is to say, at 10 atm., when the percentage rose above 0·3. But even with partial pressures of 6–8%, although there was panting, there was much less subjective distress than at atmospheric pressure, where the desire to breathe may dominate the consciousness. This lack of distress can probably be attributed to the narcotic effect of the nitrogen.

In six experiments (three of them on H. S.) the partial pressure was raised to about 4% at atmospheric pressure, and the subjects tested. Air was then added rapidly to bring up the pressure to 250 ft. in two experiments and 300 ft. in four. The partial pressure of CO_2 thus remained constant, save for that added by respiration, and may even have fallen when the observer was breathing through a CO_2 canister. The subject was then retested during the 15 min. which was the longest time spent under pressure. The mean score in the manual dexterity test at 1 atm. was 80·5, at 8·6 or 10 atm. 51·9. Fisher's t test of significance is 3·02, hence the probability that the decrease is due to chance lies between 0·05 and 0·02. In five of these experiments the arithmetic test was also used. In one the subject remained staring at the paper for 7 min. and wrote down two digits, one of which was wrong. Among those who completed it the mean percentage of mistakes rose from 28·1 to 74·4.

Four subjects were compressed from 1 to 10 atm. (300 ft.), CO_2 being added during the ascent. The partial pressure of CO_2 varied from 3·6 to 4·3%. Manual dexterity tests were then done for comparison with controls at atmospheric pressure without CO_2. The mean score fell from 59 to 43·8. $t=3{\cdot}49$, so once more the probability of a chance explanation lies between 0·05 and 0·02. In two experiments the partial pressure of CO_2 at 1 atm. was much higher, and air was added to make up 10 atm. The partial pressures of CO_2 at this total pressure were 6·3 and 7·5. The mean manual dexterity score fell from 78·5 to 55. One subject attempted the arithmetic test without being able to complete a single sum.

A number of other experiments gave the same result, namely, that the combined effects of high partial pressures of N_2 and CO_2 were much more severe than those of either alone. It will be realized that the observer was in the chamber with the subject, and had not only to add CO_2, take notes and samples, but also to supervise the tests. As a result of the increased resistance referred to earlier, and also of the effects of N_2, both observers, and especially J. B. S. H., tended to remove their respirators, or not to put them on again after speaking to the subjects. They would not have done this at atmospheric pressure, owing to the much greater subjective distress caused by a given partial pressure of CO_2. As a result their observations were often faulty, and they sometimes lost consciousness. However, another observer was stationed at the window, and it was generally possible to make out what had happened, even if notes were inadequate.

At higher partial pressures of CO_2 consciousness was lost. In almost all cases this took place quietly and easily. The subject remained sitting, leaning forward with his or her mouth and eyes open, and a glazed expression, and often salivating profusely. During the first stage of decompression consciousness was rapidly regained, and the subject could often begin writing within a few seconds, though he was subnormal for a few minutes longer. J. B. S. H. generally awoke from what appeared to him to have been a sleep, with dreams which he sometimes remembered. On one occasion he made swimming movements during recovery. The experience was in no way unpleasant. Subjects generally continued working at their assigned tasks until they lost consciousness. One subject, H. Ks., however, retched considerably and groaned while losing consciousness.

Our usual procedure was to raise the partial pressure of CO_2 by steps, beginning with a partial pressure of about 4%, which all subjects tolerated, or of 6–8%, which some subjects tolerated. On raising the pressure, consciousness was generally lost in 1–4 min.

Table 1 shows the results as regards loss of consciousness in different subjects. L. J. appears to be the most resistant individual. He had previously had 8 min. at 3·8% and 5 min. at 6·9%. In 9·8% he was not only talking rationally, but his handwriting had barely deteriorated, and his notes were entirely sensible.

It will be seen that different people lose consciousness at very different partial pressures. Probably with short exposures of this type about half a group of healthy men and women would lose consciousness at 10 atm. in 0·8% of CO_2 within 4 min. But occasional individuals would be made unconscious by a partial pressure of 6%, and a very few might survive 10%.

Table 1

Subject	Partial pressure at which conscious	Partial pressure at which unconscious	Time in minutes at highest partial pressure
L. J.	9·8	—	1
J. L.	6·8	—	3
J. N.	6·7	—	3
E. M. C.	8·1	9·7	1
H. S.	8·1*	9·7	1
J. E. J.	8·4	9·2*	4
H. Ks.	6·8	9·2	1
J. B. S. H.	7·1	8·0	1
J. M.	4·3	7·3	2
O. D.	3·7	6·8*	5
J. P.	3·6	6·6	5

* Consciousness barely lost.

It must be emphasized that this table refers to rather short exposures, this being the most interesting question for certain practical purposes. Only two experiments were done involving longer exposures. J. B. S. H. and E. M. C. were exposed to an atmosphere whose CO_2 content rose from 6·00 to 6·35% at atmospheric pressure. After 19 min. both had slight headaches, as well as hyperpnoea. E. M. C. then put on his respirator. After 21 min. the pressure was raised to 10 atm.; the partial pressure was unaltered, save for a slight rise due to respiration. After 24 min. the maximum pressure was reached, and after 32 min. J. B. S. H. was unable to take rational notes, but was rational enough to ask E. M. C.'s permission to signal for decompression, and to give the correct signal. He would probably have lost consciousness very soon. The maximum partial pressure of CO_2 was 6·5%.

In a similar experiment H. Ks. was exposed to 6·0–6·4% of CO_2 at 1 atm. for 26 min. From 30 min. onwards he was at 10 atm. pressure. After 36 min. he could not write, and began to groan loudly and retch. After 37 min. he was unconscious, but recovered at once during the first decompression. The maximum pressure was 6·8%. Thus it is probable that most people would be unable to support partial pressures of 6% of CO_2 at 10 atm. for so long as

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an hour, and we consider that, since even at 4% there was definite deterioration in manual skill after a few minutes, the partial pressure of CO_2 at 10 atm. should be kept below 3%.

The psychological effects noted under these conditions are interesting. They are well illustrated by the notes taken by H. S. during an experiment. The events are recorded in square brackets.

[11.41. Atmospheric pressure. CO_2 raised to 3·6%.]

'11.41. CO_2 let in. Sharp smell which persists. haven't noticed it before.'

[11.42. Compressed air let in.]

'11.44. Roaring in ear as in fainting begins. 11.45. Have become concicous of my change of conciouscouse. 11.46.'

[11.46. Maximum pressure reached. Hyperpnoea obvious in both subjects. 11.48. E. M. C. puts on respirator and raises CO_2 to 6·4%.]

'11.48–49. 2nd cylinder of CO_2. a few drops froze. I am still sweating but do not feel hot. Chase fanning makes me feel hyteropherateraapherea.[1] 11.48. A length of word. —— then its all over.'

[The last line was actually written at 11.52. 11.52. H. S. seems fairly good. Thinks she could do a 'ball game' if called upon. 11.53. Third cylinder of CO_2 partly emptied. H. S. has glazed look, but continues writing.]

'2nd cylingder—but I have fainted all ready.'

[11.54. H. S. looks fairly bad. Trying to write. 11.55. CO_2 8·1%. H. S. cannot fan air, but has a determined expression and is moving lips, though not talking. 11.55. H. S. unmistakably unconscious. 11.56. E. M. C. removes respirator. 11.57. H. S. twitching and blinking. E. M. C. lifts her left eyelid, and looks at her pupil. This rouses her.]

'11.259. Chase has looked at my eye under my lid to eye If they have looked if I am still still...(illegible)...still conciocous.'

[11.58½. E. M. C. lets out remainder of CO_2 from third cylinder. This is his last recollection till decompressed. 11.59. E. M. C. takes sample (9·7% CO_2). 12.0. H. S. twitching. Both look 'dopey'. 12.01. Decompression begins. 12.01½. E. M. C. writes 'Woke up from what? heard decompression in progress'.]

'12.11. We have reduced the pressure. I dont know whether I ever lost conciousness. 12.3. The last time is wrong.'

[12.5. CO_2 1·00% at 100 ft. pressure. E. M. C. at first tried to take it in tube used for last sample, which he did not remember taking.]

'12.5. I may be sick. 12.7. The headache is developing. 12.9. I am afraid of thinking about being sick. 12.9½. Feel much better. 12.14. O_2 apparatus. I am concious of gaps of time, e.g. 9·5–14. 12.17. 12.21. I think all my senses are normal, but still an effort to write. 12.22. Still a tendency to tremble. 12.24. Hear the talking outside for the first time. 12.33. 12.44. Gradually waking up.'

[1] This word was intended to be 'hypertrophied', and to mean that the effect of fanning was exaggerated by the high air density.

[12.45. E. M. C. notes 'Still very blurred mentally. Cannot remember what decompression time ought to be for 16 mins. for example.' 12.59. Emerge from chamber.]

The handwriting gradually deteriorated, and finally became very illegible, but was almost normal by 12.5 p.m. The tendency to perseveration is notable. Thus on one occasion J. B. S. H. noted 'J. B. S. H. frequently coughs because of coughing due to ? NaOH in lungs'. At the end of 32 min. in 6–6·5% CO_2, the last 8 min. being at 10 atm., J. B. S. H. tried to read the dry and wet bulb thermometers, said there was something wrong with them, and wrote down '12·08° F., 1208° F., 1288° F.' (the time being 12.8 p.m.). On another occasion E. M. C., while losing consciousness, remembers saying, 'This is eternity; everything is just the same, for ever, and ever, and ever, and ever...' and then 'hyperpnoea, hyperpnoea, hyperpnoea...'. He noticed this tendency, but was unable to control it.

However, this perseveration was only noticed in some subjects. In others the most notable psychological symptom was elation. Thus J. E. J. whilst the partial pressure of CO_2, at 10 atm., was being raised from 6·5 to 8·4% wrote, 'I feel extremely cheerful and don't mind it a bit.' 2½ min. after the CO_2 had been further raised to 9·2%, she stated when questioned, 'I feel quite O.K.' When asked to write this down, she got as far as 'I feel', but this was followed by a meaningless series of pencil strokes. She shouted 'I will write it' so loud as to be heard outside the chamber, but then began swaying from side to side and had to be supported. She probably lapsed from consciousness, and certainly did not remember what had happened; however, she stated that it had not been unpleasant.

Both the Irish subjects were elated, and laughed vigorously from time to time. One of them swore a good deal during the skill test, and was first bewildered and then amused when told that he must use one hand only (he had performed it with one hand 12 min. earlier). This subject also believed that, during the first decompression, E. M. C. took a spanner out of his hands, and said there was to be no violence. As E. M. C. has no recollection of this, and had not lost consciousness, this was probably a dream.

Other subjects were very depressed. On compression to 10 atm. at a partial pressure of 4% CO_2, one subject seized E. M. C.'s hands and said, 'I'm going to die, I'm going to die, I tell you'. On being presented with the manual dexterity test, he said, 'No, I can't possibly do anything'. However, he was reassured, and performed the test fairly satisfactorily. Another subject showed almost equal alarm.

Subjectively E. M. C., before losing consciousness, passes through a stage where it appears to him that he has always been in the chamber, and always will be, whereas J. B. S. H. sinks gradually into more or less coherent dreams. Others are unaware that they have been unconscious. Others again have gaps in their memory during which they seemed to observers to be conscious. The sense of time may be disturbed. To J. B. S. H. time seems to pass quickly.

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Similarly H. Ks., who took 28 sec. to make 30 taps (which he judged to be at intervals of a second) under normal conditions, and 32 sec. when breathing 6·4% of CO_2 at atmospheric pressure, took 60 sec. when the total pressure was raised to 10 atm.

There was often a slight headache during decompression, as is usual when the partial pressure of CO_2 is reduced at atmospheric pressure, but no subjects vomited at this stage. One (O. D.) noticed a smell of ammonia during decompression, as described by Haldane (1924) when first breathing normal air after exposure to CO_2.

COMBINED EFFECTS OF COLD AND PRESSURE

E. M. C. and J. B. S. H. lay inside the pressure chamber in a bath containing water and large amounts of broken ice. Ice was also piled as far as possible on the knees and other parts of the body emerging from the water. J. B. S. H. wore a shirt and trousers. He was comfortable for 12 min., the mouth temperature rising from 98·2 to 99·0° F., as is usual in his case. After 20 min. the teeth began to chatter, and the mouth temperature after 22 min. had fallen back to 98·3° F. After 23½ min. shivering was fairly violent, and the pressure was raised. 250 ft. was reached after 26 min. He felt much better than at the same pressure with 4% CO_2, and was able, when asked, to recite the words of a fairly lengthy song with few mistakes. The water temperature at the end was 33° F.

In a similar experiment E. M. C. wore a sweater instead of a shirt. After 12 min. he was shivering definitely, the mouth temperature remaining steady at 98·6° F. After 15½ min. he was feeling very uncomfortable, and was compressed to 300 ft. pressure, which was reached after 19 min. in the bath. He felt somewhat more comfortable. After 26 min. in the bath and 7 min. under pressure he was able to multiply 17×13 and 47×13 correctly in his head, whilst J. B. S. H., who had propounded the questions, and was taking notes, gave an incorrect answer to the latter. His mouth temperature was 98·4° F. He was decompressed during the 28th minute. Subjectively he felt 'perhaps somewhat more stupefied than he usually does at 300 ft.' during the third to fifth minute under pressure, but this passed off.

Both subjects noticed great hyperpnoea whilst breathing O_2 during decompression, after leaving the water. The shivering was sometimes so intense as to suggest clonic spasms. The O_2 consumption almost reached the maximum of 2 l. per min. permitted by the 'Salvus' apparatus, and the soda-lime canister became very hot.

It may be concluded that cold has a very slight effect, at most, in increasing the effects of N_2 narcosis. The difference between the two subjects was probably largely due to J. B. S. H. being fatter. However, it should be noted that E. M. C. is more tolerant of cold than most people.

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Combined effects of carbon dioxide and cold

When standing in a tank of water at 39° F., with much ice floating in it, immersed up to the neck, and wearing a shirt, trousers, sweater, and pants, J. B. S. H.'s teeth began to chatter after 18 min., and shivering began after 20 min., the mouth temperature being 97·3° F. He emerged after 25 min. 11 min. after emergence the mouth temperature was 98·0° F., and 23 min. after emergence the rectal temperature (normally about 99·0° F.) was 97·5° F.

After breathing air containing 5·8–6·0% CO_2 for 2 min., the same subject entered the tank, the water temperature being 38° F. The teeth began to chatter whilst taking a mouth temperature after 21 min. Chattering was in general prevented by a rubber mouthpiece. Shivering began after 26 min. He emerged after 28 min. The mouth temperature had fallen to about 93·5° F., but this was probably from breathing cold air through a mouthpiece, the tube to which was partly immersed in melting ice. The rectal temperature 4 min. after emergence was 97·2° F. There was no headache, and shivering was about as intense as in the other experiment and in comparable ones. The experiment was rather less unpleasant than usual, perhaps through a narcotic effect of the CO_2.

It had been suspected that the CO_2 might cause vasodilation, and thus lead to a much greater effect of cold. On the contrary, the skin, which normally becomes very red in cold water, was less red than usual when CO_2 was breathed. It is clear that, in this subject at least, the effects of CO_2 and cold are not cumulative, like those of CO_2 and N_2.

Combined effects of pressure, carbon dioxide and cold

J. B. S. H. immersed himself in a bath of ice in the chamber as before. The partial pressure of CO_2 was raised to 6·5%. After 17 min. the teeth were chattering and the mouth temperature was 96·7° F. The subject was not uncomfortable. The CO_2 had fallen to 6·2%, through absorption by E. M. C.'s respirator. After 19 min. shivering began, and after 20½ min. the pressure was raised, 300 ft. being reached after 24 min. J. B. S. H. coughed violently.

After 2 min. at 10 atm. his attempts to recite the same verses as before gave rise to 'short disconnected bursts of words actually occurring in the work, but in disarranged order'. After 3 min. he was making rhythmical jerking motions of the limbs, quite distinct from shivering, and after 3½ min. was quite unconscious and irresponsive. The partial pressure of CO_2 was 6·9%, having risen because E. M. C. removed his respirator.

After 4½ min. at 300 ft. the pressure was lowered to 100 ft., and consciousness was partly recovered. After 31 min., whilst getting out of the bath, the mouth temperature was 95·2° F., and 5 min. later 94·5° F. During this decompression normal consciousness was only gradually re-established, J. B. S. H.'s first impression being that the chamber was a long and com-

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paratively spacious tunnel. Whereas on three other occasions when this subject ost consciousness from the effects of CO_2 and pressure, recovery was always pretty rapid.

It may be concluded that cold somewhat enhances the combined effects of CO_2 and pressure, but it must be realized that the degree of cold was rather extreme. It is doubtful whether moderate cold would have a marked effect.

DISCUSSION

These experiments were conducted with certain practical ends in view, and we realize that they are in many ways incomplete. However, it is clear that air has a somewhat intoxicating effect at 10 atm., whilst a mixture of He or H_2 and O_2 has not. On the other hand, this effect does not get worse after the first 3 min. The further effect of CO_2 is not very great if this is calculated in terms of partial pressure. Thus, if a man were confined in an unventilated diving bell at 10 atm. he would not lose consciousness till the partial pressure of CO_2 rose to about 6%, as compared with about 10% at atmospheric pressure. As the rate of rise of partial pressure for a given metabolism is independent of the total pressure, this means that men could last for more than half as long at 10 atm. as at 1 atm.

On the other hand, if air containing 0·7% of CO_2, which has a quite negligible physiological effect at 1 atm., is compressed to 10 atm., almost everyone would be seriously affected, and probably unconscious after half an hour, whilst some people would lose consciousness at once. As against this, high partial pressures of CO_2 do not appreciably, if at all, increase the risk of symptoms arising from decompression. And it seems probable that no greater precautions against cold are needed at such high pressures than would be reasonable at ordinary pressures. All apparatus for respiration intended for use at high pressure should be tested for resistance at such pressures.

The physiology of N_2 intoxication presents some curious features. The rapidity of the onset and disappearance of the symptoms are remarkable. They are at their maximum after 2–3 min., and disappear in about the same time. On the other hand, Behnke, *et al.* (1935) find that the half-period of saturation of the body water and 16% of the lipoids with N_2 is about 7 min., that of the remaining 83% of lipoids being about 80 min. It follows that the part of the nervous system where N_2 produces its intoxicating effect must be a very vascular part, presumably the grey matter of the cortex. Thus the effects of high-pressure N_2 on the nervous system fall into two categories. The grey matter, or some of it, is rapidly saturated and desaturated. Hence the symptoms here described begin and end rapidly. But because of this rapidity of desaturation, decompression rarely causes mental symptoms, though maniacal attacks have been recorded. On the other hand, the white matter has a poor blood supply, and saturates and desaturates slowly. There is no evidence that dissolved N_2 impairs its activity in any way, though of course an exposure over many hours might have some effect. But this very slowness of gas exchange leads to bubble formation during decompression, which gives rise to paralysis, and probably to pain also. We have no explanation to offer as to why CO_2 excess and N_2 excess appear to co-operate, whilst O_2 shortage and N_2 excess do not do so to any appreciable extent. The solution of such questions waits for two things: first, a general survey of the effects of so-called indifferent gases, including the inert gases and methane; and secondly, an attempt to determine which of the biochemical processes in the brain are interfered with by N_2 under high pressure. We hope to deal, in a later paper, with the effects of O_2 at high pressure.

Summary

We confirm the finding of Behnke, *et al.* (1935) that air at 8·6 atm. pressure has a somewhat intoxicating effect on human beings, and that this effect is due to nitrogen. The nitrogen effect reaches its maximum after about 3 min. There was no reduction of manual dexterity in the test used by us, but a considerable effect on performance of arithmetic, and on most practical activities. At 10 atm. these effects were somewhat enhanced, and manual dexterity was lowered in some cases. When helium or hydrogen was substituted for nitrogen there was no intoxication.

3–4% of carbon dioxide at atmospheric pressure caused no deterioration in manual or arithmetical skill, and in the two subjects tested, 6% of carbon dioxide caused no deterioration.

When air containing about 0·4% of carbon dioxide, and therefore with a partial pressure of about 4%, was breathed at 10 atm., there was a marked deterioration in manual dexterity, and a good deal of confusion. When breathing carbon dioxide at partial pressures of 6·6–9·7% at 10 atm., eight subjects lost consciousness in 1–5 min., but some could tolerate partial pressures of over 8% for 5 min. or more. With half an hour's exposure to a partial pressure of 6–7% of carbon dioxide, one subject lost consciousness after 7 min. at 10 atm. pressure, and another nearly did so.

We consider that the percentage of carbon dioxide in air at 10 atm. pressure should be kept below 0·3%. Exposure to high partial pressures of carbon dioxide at 10 atm. does not increase the liability to 'bends' or other symptoms due to rapid decompression.

Immersion in water below 40° F. did not enhance the effects of high-pressure air, or of carbon dioxide at atmospheric pressure, but somewhat enhanced those of high pressure and carbon dioxide together.

In certain breathing apparatus the resistance became so great at 10 atm. as to be intolerable.

Few subjects experienced serious trouble during compression, or during or after decompression. But one developed a unilateral pneumothorax.

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