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PRELIMINARY OBSERVATIONS ON THE NARCOTIC EFFECT OF XENON WITH A REVIEW OF VALUES FOR SOLUBILITIES OF GASES IN WATER AND OILS

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The comparative narcotic effects of argon, nitrogen and helium have been previously studied by Behnke (1940) and by Behnke & Yarbrough (1938, 1939). Exposure up to 10 atm. of either air or an 80% argon, 20% oxygen mixture produces progressive narcotic effects in man. These effects are attributed to the dissolved inert gases, nitrogen and argon. Breathed in equivalent concentration, argon has approximately twice the narcotic effect of nitrogen and is twice as soluble as nitrogen in water and in fat. The fat-water solubility ratio of the two gases is nearly the same. Helium, on the other hand, with its lower solubility in water and fat has negligible narcotic effects when compared with argon and nitrogen.

The effect upon the central nervous system of argon, as compared with nitrogen, seems to depend primarily upon the total concentration of the dissolved gas. Reasoning from the Meyer-Overton hypothesis that anaesthetic effects are relative to the fat-water solubility ratio, it is suggested that gases such as krypton and xenon might have striking narcotic properties. These gases have a much greater water solubility and a higher fat-water solubility ratio. It is possible that 80% krypton at sea-level is as narcotic as 6 atm. of air, and that xenon under the same conditions may be equivalent to 25 atm. of air. Aside from the Meyer-Overton hypothesis, calculations of these theoretical effects are subject to considerable speculation in that the dissolved gas distribution ratio in the fat of the critical area in the central nervous system may be unlike that in olive oil. Fig. 1 shows a radio-autograph of a cross-section of a rat previously exposed to an atmosphere containing radiokrypton. After several hours' exposure the animal was killed, frozen and sectioned transversely and a section then placed in the cold, in close apposition to X-ray film. The relatively great uptake of the gas in fat containing tissue is noted by the dark areas in the radio-autograph.

A single subject in this laboratory, breathing 50% krypton and 50% oxygen in an experimental gas exchange measurement, voluntarily remarked that he had been quite 'dizzy' during the krypton inhalation. This is the report of a single subject. He had had, however, numerous experiences of breathing oxygen and nitrogen mixtures from the gasometric apparatus and, in this particular experiment, he was not aware of the fact that he was breathing some other mixture of gases.

Enough xenon was available to make a preliminary study of the effect of this inert gas upon mice. One of us (J.H.L.) exposed mice individually to a mixture of oxygen and xenon for short periods of time. The mixture was

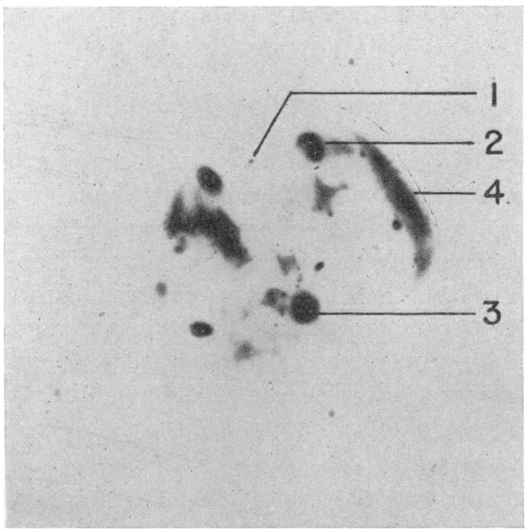

Fig. 1. The dark areas indicate clouding of the film due to radio krypton. Fat stains of section revealed those areas to have high fat content. (1) Spinal cord. (2) Perirenal fat. (3) Mesenteric fat. (4) Radiokrypton trapped in hair.

continuously circulated through soda lime, and the oxygen content frequently checked so that at least 20% oxygen was always present and CO_2 was removed. Additional oxygen was fed in as needed. The results are presented in Table 1. In the five mice exposed to an atmosphere with high xenon content, but with adequate oxygen, definite central nervous system effects were observed, and these findings might possibly be related to the high fat/water solubility ratio for xenon.

In connexion with certain studies on decompression sickness, it became necessary to know the solubilities of various inert gases in water and fats. By means of the use of radioactive isotopes, one of us (W.F.L.) determined the values for argon, krypton and xenon. An investigation of the literature and tabulation of the solubilities of various gases has given data which are of

TABLE 1. The effects on mice of breathing mixtures of oxygen and xenon, and of oxygen and krypton

No.	Gas mixture	Exposure	Narcotic effects and remarks
1	Approximately 50% krypton, 50% oxygen	1 hr.	None
2	Approximately 60% xenon, 40% oxygen	20 min.	Within 2 min. animal exhibited slight convulsive extensor movements of head. Developed weakness of hind legs. Complete recovery 15 min. after removal from chamber
3	At end of experiment 78% xenon, 22% oxygen	1 hr.	Within 2 min. mouse developed convulsive extensor movements of head; at 10 min. hind legs seemed partially paralysed; after removal from chamber had ataxia and unsteadiness with complete recovery in 15 min.
4	At end of experiment 69% xenon, 30% oxygen	1 hr.	Within 2 min. animal sluggish and convulsive. Motions of head as above. Later convulsive movements of hind legs developed
5	At end of experiment 60% xenon, 39% oxygen	45 min.	Within 2 min. developed convulsive movements of head and hind legs. On removal from chamber, ataxia for 3 min., then complete recovery
6	At end of experiment 58% xenon, 42% oxygen	30 min.	Within 1½ min. convulsive head movements as above. This continued throughout. After removal ataxia for 1 min., then apparent complete recovery

interest in the fields of aviation medicine and respiratory physiology. The results are presented in Figs. 2 and 3 and Table 2 and the bibliography is appended.

The values given are correct to two significant figures. Two or more references to a given value indicate that two or more investigators agreed (to two significant figures) to this value. Great discrepancies in the literature were found, especially in the values for neon and krypton. In cases such as these, the various figures were evaluated and those thought to be the most reliable were selected. The values for H_2, O_2, CO and CO_2 were taken from the *Handbook of Chemistry and Physics* (1944) and the *Dictionary of Chemical Solubilities* (1921). However, the *Handbook* values for the inert gases were in considerable error, having been taken from an earlier work of von Antropoff (1910). Antropoff's earlier values have been listed in the *Handbook of Chemistry and Physics* up to the 28th edition (1944), in the *Dictionary of Chemical Solubilities* (1921) and in the *International Critical Tables* (1928). Recent authors (Lannung, 1930; Valentiner, 1930; Van Liempt & Van Wijk, 1937), including von Antropoff himself (1919), have shown these values to be in error, especially those for neon and krypton. In the case of neon there seem to be only two recent sources of data—that of Lannung (1930) and that of Valentiner (1930). These two investigators differed considerably in their results, and it is difficult to decide which is the more reliable.

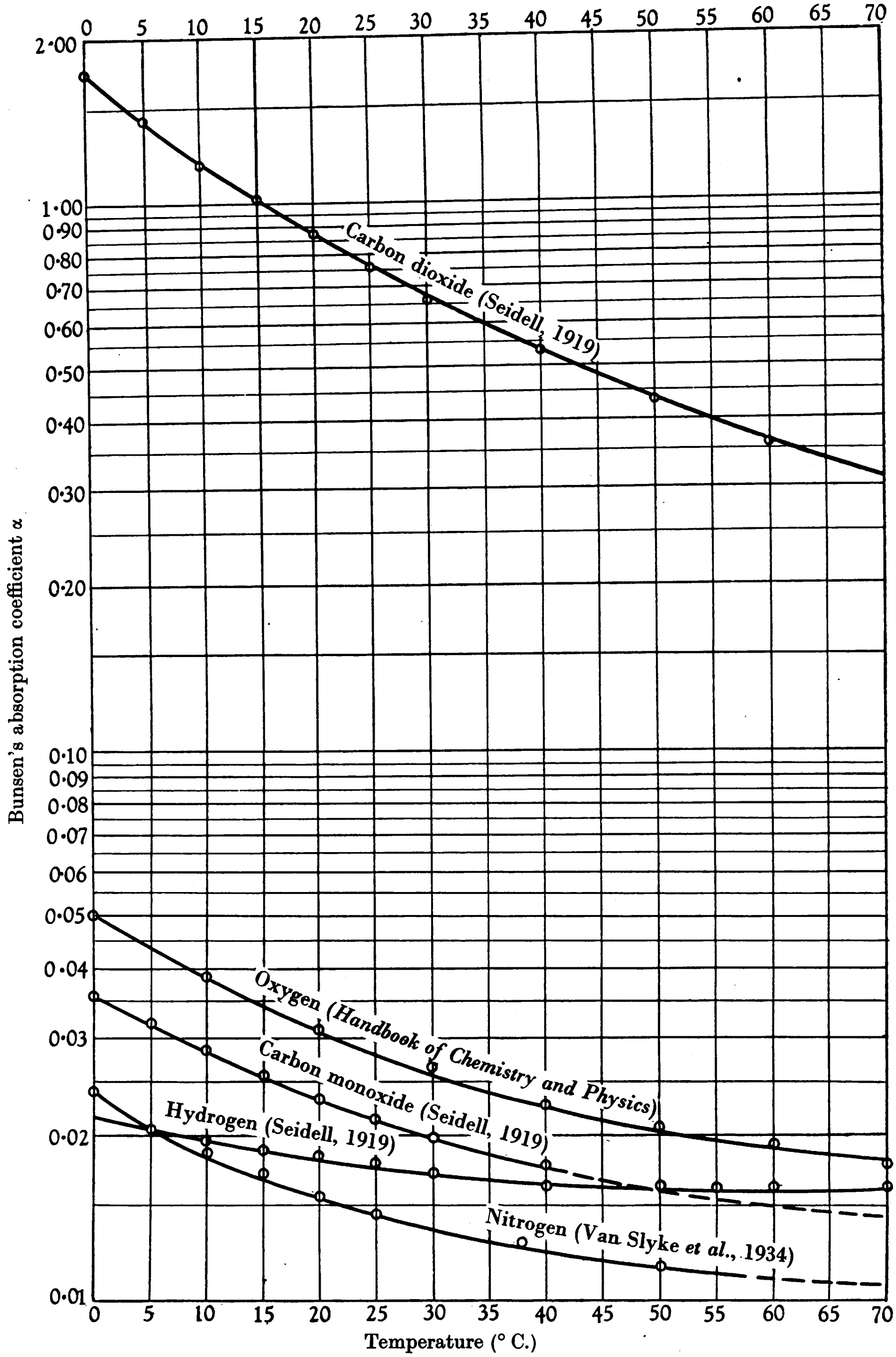

Fig. 2. Solubility of gases in water, α = c.c. gas (0° C., 760 mm.) dissolved in 1 c.c. water at temperature of observation.

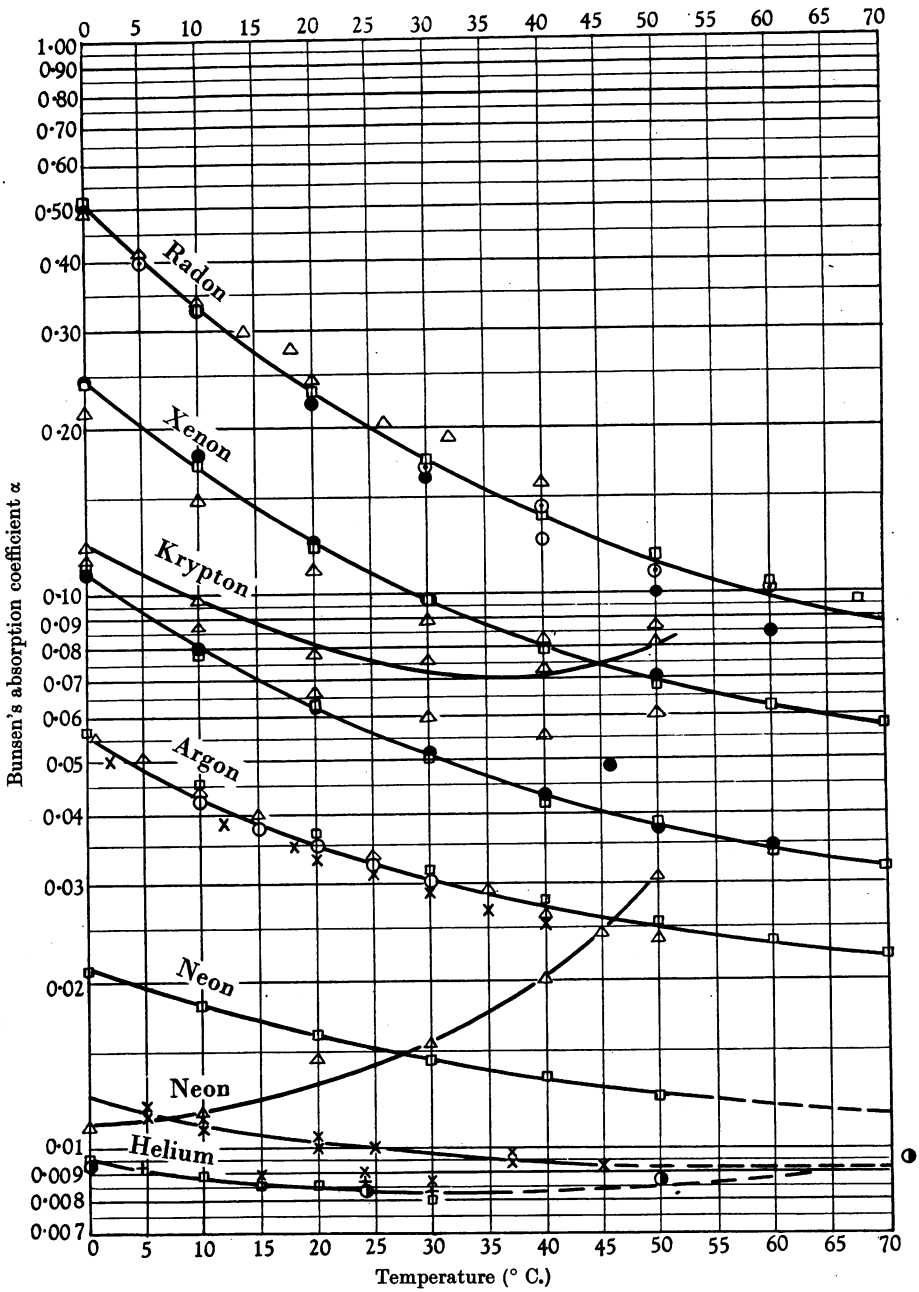

Fig. 3. Solubility of inert gases in water. ● von Antropoff (1919). △ *Dictionary of Chem. Sol.* (von Antropoff, 1910) (Argon, Comey). □ Valentiner (1927, 1930). × Lannung (1930). ○ Estreicher (1899). + Cady, Elsey & Berger (1922). ◑ Wiebe & Gaddy (1935). ⊙ Meyer (1913).

TABLE 2. Solubilities of gases in water and oils

	Gas	Mol. wt.	Half-life of isotope used	Bunsen's absorption coefficient (to 2 significant figures): Solvent, water, 22° C.	Solvent, water, 37° C.	Solvent, oil, 22° C.	Solvent, oil, 37° C.	Oil/water solubility ratio, 22° C.	Oil/water solubility ratio, 37° C.
Chemically inert gases	Helium	4	0·8 sec.	0·0086 (5, 1, 34)	0·0085 (13)	0·015 (3) olive	0·015 (3) olive		1·7 (4) olive
Chemically inert gases	Neon	20		0·0104 (15)	0·0097 (15)				
Chemically inert gases	Nitrogen	28	9·93 min.	0·015 (29)	0·013 (3)	0·052 (30) olive 0·063 (31) corn	0·07 (20) 32° paraffin 0·067 (3, 31) olive 0·063 (31) corn	3·5 olive 4·2 corn	5·2 (4) olive 4·7 (31) corn
Chemically inert gases	Argon	40	110 min.	0·037 (8)	0·026 (4, 15)	0·15* (20) olive	0·14* olive	4·0 olive	5·3 (4) olive
Chemically inert gases	Krypton	83·7	34 hr.	0·059 (28)	0·045 (33, 27)	0·44* olive	0·43* olive	7·5	9·6
Chemically inert gases	Xenon	131·3	34 days	0·13 (33, 27)	0·085 (33)	1·9* olive	1·7* olive	14·5	20·0
Chemically inert gases	Radon	222	3·825 days	0·23 (26, 19)	0·15 (26, 19)	0·25 (16) olive	0·19 (16) olive	110	125
	Hydrogen	2	—	0·018 (11)	0·016 (11)	0·042 (31) cottonseed	0·04 (20) 32° paraffin 0·05 (24) 40° cottonseed	2·3	3·1 cottonseed 2·5 paraffin
	Oxygen	32	—	0·030 (11)	0·024 (11)	0·11 (31) corn 0·11 (31) cottonseed	0·12 (24) 40° cottonseed	3·7	5·0
	CO_2	44	21·5 min.	0·83 (11)	0·56 (11)	1·34 (31) cottonseed	0·876 (24) 40° cottonseed	1·6	1·6
	CO	28	21·5 min.	0·022 (11)	0·018 (11)				

The numbers in brackets refer to the references on pp. 203–4.

* Determined in this laboratory by W. F. Loomis, using radioactive isotope.

SUMMARY

Observations on the narcotic effects of xenon are presented. The oil and water solubilities of hydrogen, oxygen, carbon dioxide, nitrogen, helium, neon, argon, krypton, xenon and radon are presented from a review of the literature and from determinations using the radioactive gases.

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