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Alterations in C.N.S. Associated with Chronic Motor Disabilities Induced by O_2 at High Pressure.

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The recovery of animals from the effects of exposure to O_2 at high pressure (OHP) is frequently remarkably rapid but residual effects commonly persist for some time after the animal's return to atmospheric pressure, varying from periods as short as a few minutes up to several days; and in some cases disabilities become permanent.[1] The post-decompressional manifestations of O_2 poisoning may then be appropriately designated as acute and chronic after-effects.

The acute after-effects are evident during the stages of decompression and the immediate post-decompressional period. These vary widely in type and intensity and in large part, may simply represent a continuation of those reactions precipitated by the OHP before decompression was begun.

The chronic effects, characterized chiefly by persistent motor disabilities and various degrees of paralyses,[1] must represent a continuation of at least some of the features of the acute after-effects. The nature of these chronic motor disabilities is highly suggestive of permanent damage to the nervous system. Yet heretofore no significant pathological changes have been demonstrated in the C.N.S. of animals which have suffered poisoning by OHP and it has been inferred that the effects of OHP on the C.N.S. are entirely "functional" in character.[2]

The failure to demonstrate lesions in the C.N.S. in poisoning by OHP[3] may perhaps be best explained by the fact that studies have been confined to the acute stages and that the induction of chronic disabilities by a single exposure is an infrequent occurrence. The fact, however, that such chronic changes can be regularly induced in experimental animals by successive exposures to OHP, should provide particularly good opportunity for demonstrating any changes which OHP might possibly induce in the C.N.S.

An investigation was therefore begun to determine what alterations, if any, might be found in animals in which chronic motor disabilities were induced by successive exposures to O_2 at pressures of about 65 pounds (gauge). The exposures, for the most part, were made 3 times per day, but neither the duration of each nor the total number employed, was uniform for all animals. This lack of uniformity in all experiments was occasioned by the individual variations in the susceptibility and by the desire to induce various degrees of severity of chronic involvement. The greater number of the exposures, however, were of about 20 to 30 minutes duration and the total number of exposures in any one series varied from as few as 4 up to 30.

Decompression was carried out in stages and occupied a period of time equivalent to that of the duration of the exposure to the increased O_2 pressure. This relatively slow decompression eliminated possible complications from O_2 bubble formation, although according to some authors such precautions are quite unnecessary. When the desired severity of chronic neuromuscular disability had been induced and had persisted for some time the animals were killed by cardiac puncture and the C.N.S. removed for histological study.

Microscopic examination of the C.N.S. tissues revealed the following significant points: congestion, perivascular oedema, oedema of the white matter, and focal areas of anemic necrosis. Neuropathological examination in other animals revealed definite pathology characterized by a softening of the white matter; and degenerative changes. The C.N.S. of those animals which succumbed shortly after a

1 Bean, J. W., and Siegfried, E. C., *Fed. Proc.*, 1943, **2**, 2.

2 Smith, L., *J. Physiol.*, 1899, **24**, 19.

3 Shilling, C., and Adams, B. H., ... 1931, **31**, 112.

single, or the first few exposures, showed no significant alterations from that of the controls; the same was true of those which, while they were subjected to more exposures, were killed shortly after the occurrence of motor disability. It would appear therefore that animals must survive the C.N.S. injury induced by successive exposure to OHP for some time in order to permit the development of demonstrable cytological changes. This supports the explanation, mentioned above, for the failure of earlier investigations to demonstrate parenchymal damage to the C.N.S. in poisoning by OHP in more acute exposures. Further detailed examination of C.N.S. changes in a longer series of experimental animals now in progress provides confirmatory evidence that successive exposures to OHP cause irreversible damage of degenerative character in tissue of the C.N.S., especially in nerve fiber tracts, and that it is this damage which is responsible for the chronic motor disability observed in animals following successive exposure to OHP.

It has long been known that exposure to OHP causes congestion in various organs of the body, but the finding of especial interest here is that of the injury to the parenchyma of the C.N.S. The occurrence of this tissue damage in animals suffering chronic neuromuscular disabilities as a result of exposure to OHP together with the likelihood that such tissue injury is an extension of some of those etiological factors responsible for the acute after-effects suggest that some of the acute reactions themselves are manifestations of less severe and reversible tissue injury.

The cause of the tissue injury, regardless of its severity and degree of reversibility, must lie in some transient influence. This may well be a combination of the increased CO_2 tension in the tissues, the accompanying increased tissue Ch and a direct action of OHP on cellular enzyme mechanisms, all of which conditions obtain in exposures to O_2 at high pressure. The postulation of a special toxic substance and its persistence after the return of the animal to atmospheric pressure not only lacks experimental support[2,4,5] but also appears to be unessential to explain the reactions which occur during and after exposure to O_2 at high pressure. But in any case the observation that exposure to OHP induces demonstrable tissue injury within the C.N.S. seriously questions the contention that the nervous manifestations of poisoning by OHP are entirely "functional."

The author wishes to express his appreciation to Drs. Wanstrom and Parsons, Department of Pathology; Dr. Loewenberg of the Neuropathological Institute, and to Dr. Crosby of the Neuro Anatomy Department for their help in the examination of the tissues concerned in these experiments.

4 Campbell, J. A., *Brit. J. Exp. Path.*, 1937, **18**.

5 Bert, P., *La Pression Barometrique*, G. Masson, Paris, 1878.

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Development *in vitro* of Penicillin-Resistant Strains of the Gonococcus.*

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It has been demonstrated that certain strains of the staphylococcus, the streptococcus, and the pneumococcus acquire resistance to penicillin when grown in broth containing increasing concentrations of the drug. Abraham and his colleagues[1] were able in 16 weeks to adapt a strain of *Staphylococcus*

* This study was financed by a grant from the Ortho Research Foundation, Linden, N.J.

1 Abraham, E. P., Chain, E., Fletcher, C. M., Gardner, A. D., Heatley, N. G., Jennings, M. A., and Florey, H. W., *Lancet*, 1941, **2**, 177.