Thyroid in Pulmonary Injury Induced by O_2 in High Concentration at Atmospheric Pressure.* (19990)

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Hypophysectomy has been found to afford a very appreciable measure of protection against the pulmonary damage which O_2 at high pressure of several atmospheres (OHP) (1) and in high concentrations at atmospheric pressures(2) inflicts in animals exposed thereto and there is very convincing evidence that such protection is in part at least due to the elimination of adrenocortical influences consequent upon the absence of the adrenocorticotropic substances(2,3). Thyroid activity is diminished in hypophysectomized animals and since the adverse effects of exposure to OHP are so intimately related to metabolism especially to the production and accumulation of CO_2 in the tissues, it was of interest, to determine what effect the administration of thyroid might have on the adverse pulmonary reaction to O_2 in high concentration at atmospheric pressure in both normal and hypophysectomized animals. To this end the experiments described below were carried out.

Procedure. Young male albino rats of about 120 g body weight were used as experimental animals. The feeding of desiccated thyroid (20 mg per rat per day) was begun 7 days prior to and continued during the period of exposure. The exposures to O_2 in concentrations of 94% and above at atmospheric pressure were made in a chamber which provided for the continuous absorption of CO_2, which as analyses showed did not exceed 0.1% except in one instance when it rose to 0.3% for a short interval. The temperature was maintained at that of the room or slightly above. A control group of normal and hypophysectomized animals was maintained under identical conditions in the air at atmospheric pressure. The criteria of the adverse effects of the increased O_2 was the general behavior of the animals, their survival times and the post mortem macroscopic pathological changes in lungs, thorax and liver.

Results. In the first series of experiments in which 11 animals were exposed, it was found that the non-hypophysectomized animals which had been fed thyroid were the first to show ill effects; they became hyperpneic and lethargic at about the 20th hour of exposure. These symptoms increased to dyspnea and coma and the animals succumbed at about the 46th hour. The next to succumb were the non-hypophysectomized animals which had been fed no thyroid; the symptoms in these were essentially the same as those of the thyroid fed animals but their onset was somewhat later and they succumbed at about 56 hours. These data indicate, therefore, that thyroid had distinctly augmented the susceptibility of the normal rats to the adverse influence of the increased concentration of O_2 at atmospheric pressure. The third in order of onset of symptoms and death was the group of hypophysectomized animals which had been fed thyroid. They succumbed at an average of 66 hours of exposure. By far the most resistant were those hypophysectomized animals which had been fed no thyroid; only a part of these reached a severity of terminal states at the end of 96 hours of exposure at which time all were sacrificed. These procedures were repeated in a second experimental series of 13 animals. Seven hypophysectomized and four non-operated animals were exposed to the increased O_2 and controls for these were exposed to air at atmospheric pressure. The separation of the effects on the various groups was not quite as sharp as in the first experimental series but the results were in essential agreement therewith.

In both of these experimental series the post mortem examination of the thoraces, lungs and livers of animals which had succumbed to the increased O_2 or were sacrificed in terminal states revealed in various degrees the typical macroscopic changes described elsewhere as result of increased O_2(2,3);

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massive hydrothorax with a clear, watery, bloodless solution which clotted on standing, pulmonary congestion, hemorrhage, oedema and hepatization so that the lungs frequently sank in fixing solution; the liver was enlarged and congested as were also the adrenals in the non-hypophysectomized animals. In the non-operated animals all of these changes were markedly more severe in the thyroid fed animals than in those not having been fed thyroid. Similarly, in the hypophysectomized animals, thyroid feeding enhanced the susceptibility to these pathological effects so that it approximated that of the normal non-thyroid fed animals, whereas the hypophysectomized animals not receiving thyroid remained relatively free of the more severe changes. Clearly, thyroid feeding augments the susceptibility to the pulmonary damaging effects of increased O_2 in the normal animal and counteracts to large extent the protective action which hypophysectomy affords against these effects.

Discussion. The importance of CO_2 as a causative agent in the reaction of animals to O_2 at high pressure is well recognized(4-9) and the disruption of the carriage of the CO_2 by the hemoglobin in such situations results in an elevation of tissue and blood CO_2 and an increased acidity(5,10). It is held by some authors(11,12) that the cause of the pulmonary damage by O_2 at atmospheric pressure is an elevation of blood CO_2. If this latter be so, the effects of thyroid feeding seen in our present experiments might simply be explained as being due to an additive effect of a further CO_2 elevation in tissue and blood as a result of increased O_2 metabolism. But the small elevation in blood CO_2 would, by itself, appear to be insufficient to fully explain the pulmonary damage. It is highly probable that increased O_2 has an adverse effect of its own and renders the tissue peculiarly susceptible to CO_2 changes.

Taken as a whole the experimental evidence points to a multiplicity of factors which contribute to the over-all picture of pulmonary damage, hydrothorax and liver involvement induced by exposures to O_2 in high concentrations at atmospheric pressure and calls for further investigation.

Summary. 1. In a study of the influence of O_2 in high concentrations (94% at atmospheric pressure) it was found that the administration of desiccated thyroid augments the adverse effects of O_2 on normal and on hypophysectomized rats as shown 1) by a shortening of both the onset of the symptoms—hyperpnea, lethargy, dyspnea, coma—and the survival times, and 2) by increasing the severity of macroscopic *pathological changes*, including massive pleural effusion and hydrothorax, congestion, oedema and hepatization of the lungs and enlargement and congestion of the liver. 2. The pronounced protection which hypophysectomy provides against the adverse pulmonary effects of increased O_2 is in large degree counteracted by the administration of thyroid to the hypophysectomized animal. This protection is, therefore, attributable not only to the loss of adrenocortical principles but also to the loss of thyrotropin. The possible involvement of an increased CO_2 in the thyroid effects is discussed.

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