and abnormal mitoses. They were non-viable as demonstrated by their failure to grow after transfer into new mice. Moreover, the exudate of treated mice contained numerous macrophages loaded with clumps of colloidal gold(3). In untreated controls the growth of free tumor cells in the exudate resulted, as a rule, in their implantation into mediastinum and later on in abundant growth of these implants. Only small nodules, often consisting of necrotic tissue, were found in treated animals. (3) Intrapleurally injected colloidal Au^{198} was largely stored in the thoracic cavity (in macrophages and in lymphatic tissue), mainly in the mediastinum, but nevertheless it reached the liver and the spleen in considerable amounts. However, it was found that ratio $\frac{T}{A}$ (index of Au^{198} distribution between thoracic and abdominal tissues) could be increased by the use of small doses for intrapleural injection of Au^{198}(5). Infiltration of thoracic tumors with intrapleurally injected Au^{198} was noted. (4) It is concluded that irradiation with intrapleurally injected Au^{198} induced degeneration and disintegration of free tumor cells in the pleural exudate. It is presumed that inhibition of tumor cell implantation was the result of radiation damage to implanted tumor cells (direct effect) and to the tumor bed (indirect effect on tumor growth).

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Pulmonary Edema in Oxygen Poisoning.* (19614)

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In the majority of investigations on pulmonary edema associated with oxygen poisoning, the criteria for the evaluation of the degree of the edema have consisted of gross and microscopic examination of the lungs or lung sections removed at autopsy(1-3). The gross examination has consisted of an approximate estimate of the size and texture of the extirpated lungs, the color, the presence of foam in the airways and the determination of whether or not fluid exudes from a cut surface. In order to supplement this usual pathological examination and to provide quantitative numerical data suitable for statistical evaluation, a method of lung analysis has been devised which will evaluate factors useful for determining the degree of pulmonary edema (4). This new method, which consists of a chemical and physical analysis of lungs extirpated at necropsy, has been used to determine quantitatively the degree of pulmonary edema following exposure to pure oxygen at ground level barometric pressure.

Methods. A group of 7 to 9 healthy guinea pigs of approximately the same size were selected and placed on the same dietary regime in the same laboratory for a period of 2 to 3 weeks. At the end of this period, 2 animals (controls) were killed and their lungs ana-

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TABLE I. Changes in Means and Stand. Dev. of Lung Measurements during O_2 Poisoning.

Duration in O_2, hr	No. of animals	L/B, g/mg	L/IPN, g/mg	SPN/IPN, g/mg	Hb/IPN, g/mg
0 (controls)	9	7.15 ± 1.15	.113 ± .017	.91 ± .05	2.47 ± .54
36–60	5	8.61† ± 1.03	.127* ± .018	.99* ± .24	2.82* ± 1.21
60–83	10	14 ± 5.9	.186 ± .056	1.71 ± .65	1.92* ± .60
84–108	10	16.1 ± 4.4	.198 ± .076	1.71 ± .65	3.25* ± 3.5
108–132	4	19 ± 5.3	.181 ± .031	1.45 ± .44	2.65* ± .44

* Not significantly different from control.

† Significantly different from control at 10% level; all other values significantly different from control at less than 1% probability.

lyzed. The remaining animals of the group were placed in an "oil-drum" type sealed gas chamber containing soda lime racks, and into this chamber a stream of pure oxygen was passed through an inlet tube. An outlet tube permitted escape of chamber gas which was periodically analyzed for oxygen and carbon dioxide. After 24 to 48 hours, one or more guinea pigs were removed, sacrificed and their lungs analyzed. During the succeeding 3 or 4 days the remaining animals were removed, with no animal remaining more than 6 days in the oxygen atmosphere. After 4 days in oxygen the animals commenced to die and any dead animals were rejected. After removal from the chamber, the animals were immediately and quickly killed by guillotine, the chest opened and the lungs removed. This operation required about 2 to 3 minutes. The procedure for lung analysis has been described previously(4), as well as values for a large series of normal guinea pigs(5). After removal and trimming of the lungs, they were weighed. The lungs were then ground to a pulp in sand and extracted until colorless with 1% NaCl solution. The insoluble residue was analyzed by the Kjeldahl procedure for nitrogen, and this fraction, which consists of nitrogen in the insoluble protein of lung framework, pulmonary vessels and parenchyma, is designated as the insoluble protein nitrogen fraction. The saline extract contains the soluble protein, including hemoglobin. An aliquot of the extract was dried and the dried residue extracted with an ether-alcohol-acetic acid mixture, which provides a clear solution of acid hematin. Another aliquot of the saline extract is treated with tungstic acid to precipitate protein which is determined by the Kjeldahl procedure. The soluble protein, other than hemoglobin, is determined by difference. In one group of guinea pigs the lungs were removed and sections prepared for histological examination. The sections were prepared either by staining with aniline blue and chromotrope for erythrocytes or by treatment with periodic acid and staining with Schiff's reagent, which reveals acidophilic fibrinoid material.

Terminology. The following abbreviations will be used. The lung weight measured in g will be designated as L, and the body weight (kg) designated as B. The lung weight:body weight ratio is L/B. The insoluble protein nitrogen fraction (mg) is IPN, and the soluble protein nitrogen fraction (mg), SPN. Pulmonary hemoglobin (mg) is designated as Hb.

Results. Results of the analyses are given in Table I. The animals have been arranged in groups according to the duration time in oxygen, which is given in the first column. The values in the table are the means and standard deviations for each group. The first row of numerical values in the table contains the control data for the animals not exposed to oxygen. For the animals exposed to oxygen, the significance of variation from the control values has been computed, using the method described by Snedecor(6). Fig. 1 contains the individual values of L/B, and Fig. 2 the values of L/IPN from 6 experiments, each of which used 7 to 9 guinea pigs. These figures reveal the variability in the congestive edema which is particularly noticeable after more than 48 hours of pure oxygen breathing.

Discussion of results. After 48 hours of exposure to oxygen, symptoms of pulmonary edema commence, and the condition increases progressively until death occurs after 4 to 6

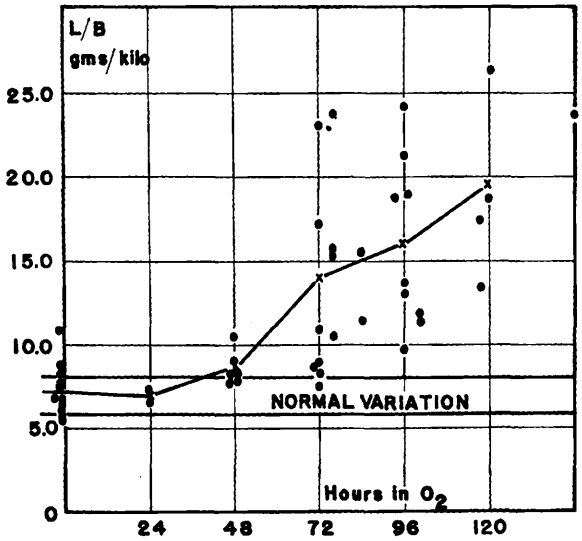

FIG. 1. Variation of (lung wt)/(body wt) ratio after exposure to pure oxygen for varying exposure duration times.

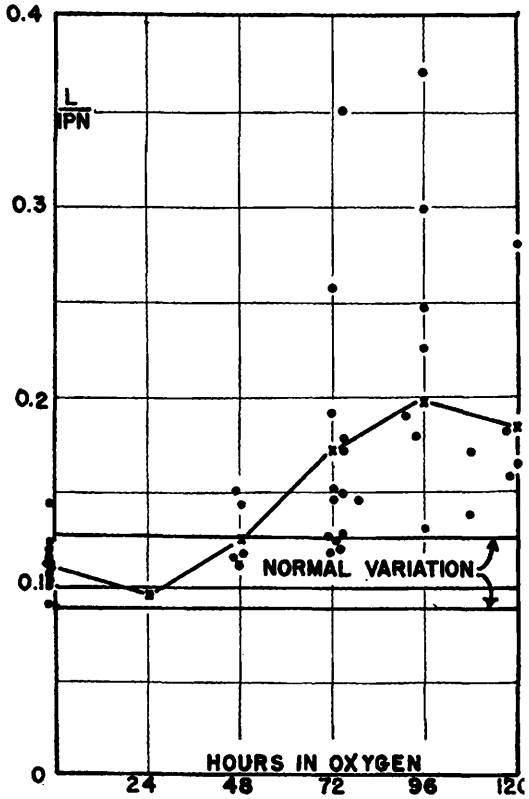

FIG. 2. Variation of (lung wt)/(insoluble protein nitrogen) ratio after exposure to pure oxygen for varying exposure times.

days of pure oxygen breathing. The lungs increase in size with the lung weight/body weight ratio more than doubling. There is considerable variability between values, but the changes are highly significant. The fraction IPN is a fraction which does not change appreciably with the onset of acute edema. The insoluble protein nitrogen contains the protein nitrogen of the lung framework and parenchyma. If acute congestive edema is considered as an invasion of pulmonary tissue by fluid containing plasma protein and hemoglobin, then the IPN fraction will not increase, while SPN and Hb should increase. It has been shown previously(5) that there is close correlation between lung weight and insoluble protein nitrogen of normal guinea pigs; hence the IPN fraction can be used as an estimate of the size of the non-edematous lung, and from relations previously established for normal guinea pigs, the predicted normal values of both SPN and Hb can be obtained. If L/IPN increases above normal, this value can be used as a quantitative measure of the edematous process and can be considered as an estimate of the increase in lung weight. SPN/IPN can be considered as a measure of the increase of soluble protein in the edematous lung. Likewise, an increase in Hb/IPN will indicate quantitatively the increase in pulmonary hemoglobin and will be a measure of the pulmonary "congestion." It is to be noted that the ratio L/IPN increases signifi-

cantly after 60 hours of oxygen breathing from a control value of 0.113 to a value of 0.198, an increase in the ratio of approximately 75%. The increase in SPN/IPN from the control value of 0.91 to 1.71 represents an increase of soluble protein in the lung to a value almost double the normal value.

Although most observers report "bloody lungs" as a result of oxygen poisoning, the results obtained in this present study do not indicate a pulmonary hemoglobin significantly higher than normal. The mean values of pulmonary hemoglobin in 3 of the 4 experimental groups increase, but the variability, both in controls and in oxygen poisoning groups, is so great that the changes are without significance. In one group, namely, the group subjected to pure oxygen for 60 to 83 hours, the Hb/IPN value was 1.92, this being lower than the control mean of 2.47.

Histological examination of the sections stained for erythrocytes revealed in some cases extensive invasion of the alveoli and interstitial spaces with erythrocytes. This would indicate that in some lungs or parts of lungs there is extensive congestion. When, however, the entire lung is analyzed, the pulmonary hemoglobin is not significantly raised. This would lead to a conclusion, supported also by visual examination of the lungs, that congestion was not uniform throughout the lungs, but localized in regions. An interesting observation also noted by Karsner(2) and Barach(7) was the finding of an increase in "fibrinoid" material after oxygen poisoning.

Conclusion. When guinea pigs are placed in an environment of 95 to 99% oxygen at ground level barometric pressure 73 to 75 cm Hg, the animals will develop pulmonary edema as a symptom of oxygen poisoning after 48 hours. The condition becomes progressively worse, and the animals die after 4 to 6 days in the oxygen atmosphere. Lung analyses during severe oxygen poisoning indicate an approximate doubling in lung weight and soluble protein nitrogen. Pulmonary hemoglobin, while quite variable in amount in different lungs, does not increase significantly in the entire lung during oxygen poisoning, but local regions, as shown by histological examination, may be intensely congested.

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Uptake of Radioactive Sulfur by Chondrosarcomas in Man. (19615)

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The ground substance of cartilage contains sulfuric esters of polysaccharides. Dziewiatkowski has shown that the radioactive sulfur of labeled sulfate given to rats is fixed by cartilage(1) and incorporated into chrondoitin sulfuric acid(2). The other tissues of the rat retain S-35 in smaller amounts and for shorter periods(3). There is little exchange between inorganic sulfur and the sulfur of amino acids and proteins(4), so that the major portion of the labeled sulfate given to rats is excreted within 24 hours(3). In man the excretion is somewhat slower(5). It is known that some differentiated tumors have metabolic patterns similar to those of the tissue of origin. Metachromatic staining properties indicate specifically the presence of sulfuric esters of polysaccharides(6) in the ground substance of