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The Mechanism in the Development of Pulmonary Edema.

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In a paper recently published, Johnson[1] gives an account of 2 sets of experiments in which it was possible to prevent the development of pulmonary edema which otherwise would have occurred following the injection of adrenalin and caffein in rabbits. The first method consisted in the opening of the chest wall. In experiments independently carried out by both the writer in association with Dr. M. S. Fleisher, and by Dr. Johnson, the occurrence of pulmonary edema was prevented by this procedure. The second method consisted in the insufflation of air into the lung. Dr. Johnson attributes the prevention of pulmonary edema in these cases to increased pressure exerted on the walls of the capillaries of the lung acting in the direction from the alveoli towards the pleural surface. This increased pressure on the vessels tends to compress them and to counteract the increased pressure which obtains in the lumen of the vessel which latter is caused by the obstacle to the outflow of blood from the pulmonary veins produced by the spasm of the left ventricle and contraction of the peripheral arterioles. We believe that these considerations are of significance in the analysis of pulmonary edema and that the pressure exerted on the pulmonary vessels is an important factor in edema of the lung, but we suggest a modification in the definition of the manner through which the outside pressure acting on the pulmonary vessels influences the development of edema.

We believe that in the experiments of Dr. Johnson as well as in other cases of pulmonary edema the negative pressure which develops in the pleural cavity as well as in the alveoli of the lung during the phase of inspiration tends to suck out the fluid from the vessels concomitantly with the sucking of the air from the outside into the alveoli. The more intense the inspiratory movements are, the greater the tendency to withdraw fluid from the blood, provided other conditions make such a transudation possible. There are various factors which fulfill the latter condition, namely, (1) the overdistension of the pulmonary vessels, probably associated with increased blood pressure following injection of a large amount of adrenalin, or of a small dose of adrenalin combined with caffein. (2) An increased permeability of the pulmonary vessels, perhaps associated with inflammatory congestion, as the result of the inhalation of irritating gases. (3) In case the entrance of air into the alveoli of the lung is inhibited through occlusion of the bronchi or trachea, the occurrence of pulmonary edema is due to increased inspiratory efforts and to increase in the negative pressure in the alveoli, and subsequent increase in the sucking force acting on the capillary blood in the walls of the alveoli and aspirating the fluid into the alveolar spaces.

All those measures which diminish the negative pressure during inspiration and the consequent sucking action should prevent pulmonary edema or at least decrease its intensity. Both the methods employed by Dr. Johnson, namely, admitting air from the outside through an opening in the chestwall as well as insufflation of air through the trachea, may thus be expected to diminish the negative pressure in the alveoli during inspiration and diminish pulmonary edema. We believe, therefore, that it is not only the dilatation of the vessels and the subsequent increase in permeability of the vessels which have to be considered in this connection, but also a direct aspirating effect, developing as the result of negative pressure, on the fluid in the dilated vessels, and this sucking effect should be expected to take place during inspiration.

In the case of pleural effusions, Graham[2] has suggested that the negative pressure obtaining within the thoracic cavity during inspiration might force out the fluid into the pleural cavity. However, in this case, experiments *in vitro* by Graham showed an actual squeezing out of the fluid to occur during the expiratory phase. The conditions determining the production of pleural effusion under the conditions obtaining *in vitro* and the formation of pulmonary edema in the living animal are not identical. Our conclusions are in accord with the findings of Auer and Gates,[3] who observed that in

rabbits in which the vagus has been cut, insufflation of air into the bronchi prevented edema of the lung, and who attributed this effect to the diminution in negative pressure during expiration. These authors believe that negative pressure is an important factor in the development of pulmonary edema. We conclude that also the opening of the chest prevents or diminishes edema of the lung by this same mechanism.

[1] Johnson, Scott, PROC. SOC. EXP. BIOL. AND MED., 1927, xxv, 181.
[2] Graham, E. A., *J. Am. Med. Assn.*, 1921, lxxvi, 784.
[3] Auer, John, and Gates, F. L., *J. Exp. Med.*, 1917, xxvi, 201.

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The Specific Action of Salts in Preparation of Urease from Amoebocyte Tissue of Limulus.

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In previous investigations Loeb and Bodansky[1] found that different salts have a specific action in the extraction of urease from amoebocyte tissue of Limulus, in accordance with the character of the kations. The salts of alkaline earths are by far the most favorable; the salts of alkali metals are very unfavorable, and the salts of Mg and in decreasing order Mn are intermediate in effectiveness. While extracts prepared with salts of heavy metals are apparently of similar strength to those prepared with salts of alkali metals, the addition of the salts of heavy metals to active extracts is very much more injurious than the addition of salts of alkali metals.

We recently analyzed the effect of mixtures of salts in the preparation of the urease, and the effect of addition of salts after the extraction with certain salts had been completed. If mixtures of salts are used in the preparation of extracts, the activity of the extracts thus prepared is approximately intermediate between the activity that is characteristic of each component salt; this applies to various combinations of NaCl, $MgCl_2$ and $CaCl_2$. If on the other hand, the extraction is first completed and then another salt is added, the results vary in accordance with the salt used for extraction. If we extract with NaCl and add a more favorable salt to the extract the addition of the latter salt is ineffective. On the other hand, if the extract has been prepared with $MgCl_2$, the subsequent addition of $CaCl_2$ leads to a condition in which the activity coefficient is inter-