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Correlation of Mechanical Properties of Infant Lungs with Surface Activity of Extracts.* (27205)

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Much so-called elasticity of lungs is due to forces acting at the surfaces of small terminal air spaces, and is modified by presence at the gas-liquid interface of a film of surface-active material. Such material extracted from normal lungs has the property of changing surface tension to a great extent when surface area is changed(1). This property has been assumed to be related to the hysteresis characteristically present in pressure-volume curves of lungs when inflated with air (but absent when filled with saline) and to the stability of aeration of the lungs in expiration. The material presumably responsible for altering surface tension has been called "anti-atelectasis factor"(1).

In lungs obtained from newborn infants (both stillborn and those that lived a short period), there are high incidences of poor stability of aeration when artificially expanded and of decreased surface-activity in extracts examined with a surface balance of variable area. Similar information about a smaller volume of more diverse material was reported recently(2).

Numerical indices have been calculated for lung stability (L) from the deflation part of the pressure-volume (P-V) curve and for extract activity (*S*)¶ from the compression part of the tension-area curve. The lung stability index is:

$$L = \frac{V_5 - V_0}{V_M - V_0} + \tfrac{1}{2}\frac{V_{10} - V_0}{V_M - V_0}.$$

V_M denotes maximum lung volume, V_5 and V_{10} the volumes at 5 and 10 cm H_2O and V_0 the volume of trapped gas at 0 cm H_2O. L varies between 0 and 1.5. Specimens tending to collapse on return to low pressure have low values of L. The extract activity index is defined as change of surface tension divided by average surface tension(2):

$$S = 2\ (\gamma_{max} - \gamma_{min}) \ /\ (\gamma_{max} + \gamma_{min})$$

γ_{max} and γ_{min} denote maximal and minimal surface tensions of the extract. *S* lies between

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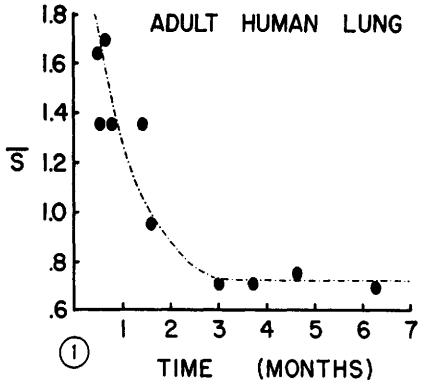
¶ *S*=S with diacritical mark in Fig. 1 and 2.



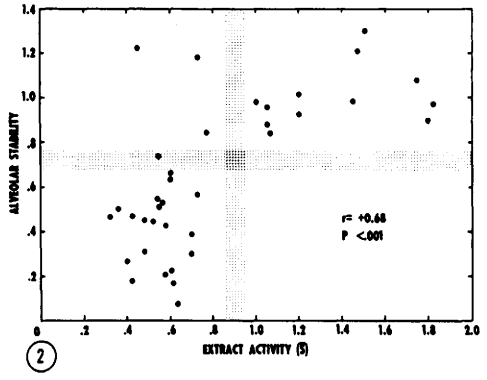


FIG. 1. Decrease in activity of an extract of one lung kept frozen (−20°C) for varying lengths of time. *S* is an index of change of surface tension divided by the avg tension.

FIG. 2. Correlation of alveolar stability (L) as calculated from pressure-volume curves with extract activity *(S)* of the same specimens.

0 and 2. Increase in surface-activity increases the alteration of tension by change in surface area and decreases the average tension.

During refrigerated storage, a highly surface-active preparation lost about 50% of its activity within about 2 months (Fig. 1). Therefore, only those cases in which surface-activity of the extract was examined within 6 weeks after autopsy were considered satisfactory.

Fig. 2 shows L and *S* plotted against each other for all infant lungs on which both examinations were performed satisfactorily. The lines dividing the graph are drawn to indicate areas of good and poor stabilities. If high surface activity were the cause of high pulmonary stability, then high values of L and *S* should be associated. Conversely, low values of L and *S* also should be associated. This is the case, the majority of points lying in the first and third quadrants. The correlation coefficient between L and *S* is + 0.68, with $P<.001$. There are no cases with high *S* and low L. The reverse, low *S* and high L, was found in only 3 cases. One can thus make the statements that when lung stability is poor, surface-activity of the extract will be low and, conversely, that when extract activity is high, lung stability will be good. The corollary, that when lung stability is good, extract activity will be high, has 3 exceptions. These are due probably to deterioration of the extract, or of tissue to be extracted, during periods of preservation before estimation of extract activity. All P-V curves were done promptly. These results are consistent with the hypothesis that stability of expansion is due to the high surface-activity of the alveolar lining film.

Present knowledge of the significance of poor lung stability and low surface activity of extracts in spontaneous human disease is limited to the perinatal period. In liveborn infants these observations are frequently associated with the respiratory distress syndrome and its pathologic corollary, hyaline membranes in the lungs(3). In stillborn infants, there is a similar incidence of low L and *S*. This has been thought to indicate a predisposition to the respiratory distress syndrome(4). Since *S* indicates activity, rather than the presence or absence of surface-active material, this material may be present, but inactivated, in the lungs with poor stability.

Summary. Elastic properties of lungs of newborn babies vary greatly, as indicated by pressure-volume measurements on post mortem specimens. The surface-activity of saline extracts prepared from such specimens also varies considerably. Indices expressing these two characteristics are significantly correlated in 37 cases. Deficiency or inactivation of an "anti-atelectasis factor" may be responsible for poor aeration of lungs in many newborn children.

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Antigenic and Anaphylactoid Studies with Seromucoid and Seroglycoid.* (27206)

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Many agents are known to produce an anaphylactoid reaction in rats characterized by hyperemia, cyanosis and edema. Included among these are such diversified substances as dextrans(1), 48/80(2), hyaluronidase(3), polymyxin B(4), egg white(5), etc. The latter has been studied extensively and it has been established that the ovomucoid fraction is the causative factor(6). Since ovomucoid is classified as neutroglucoprotein, the study of neutroglucoproteins obtained from serologically different species might be of value in identifying a common moiety capable of engendering the hypersensitivity reaction. Equine seromucoid and bovine seroglycoid were used.

Materials and methods. Equine seromucoid (ESM) was prepared from serum according to the method of Rimington and Van den Ende(7). The following modification facilitates the subsequent removal of pigment: solid sodium bromide was added to one liter of serum until a specific gravity of 1.21 was reached. The resulting solution was centrifuged at 20,000 rpm for 12 hours and the supernatant layer, essentially containing the lipoproteins, was discarded. The residue was dialyzed against running water until free of bromide and further diluted to make a volume of 4 liters. After adjusting the pH of the solution to 4.7 with acetic acid, the mixture was heated until coagulation was complete following which the pH was readjusted. The coagulum was filtered off, the water-clear filtrate concentrated to a small volume and precipitated by addition of 2 volumes of 95% alcohol. The precipitate was collected by centrifugation, washed several times with absolute alcohol and then with ether. Further purification is not necessary for this technic results in a product which is white and not contaminated with yellow pigment.

Bovine seroglycoid (BSG), which is carried down with the albumin precipitate, was generously supplied by Mann Research Laboratories, New York City.

Two sets of experiments with rats were carried out: the first consisted of intact, white females of about 150 g in weight, and the second of comparable white females which were bilaterally adrenalectomized 24 hours prior to challenge. The rats of each group of 4 received 3 mg ESM or BSG in 1 ml saline given intravenously.

Results and discussion. None of the rats in either the intact or adrenalectomized groups exhibited any evidence of an anaphylactoid response to either ESM or BSG.

The anaphylactoid reaction in the rat is believed to be a response to histamine and/or serotonin released from degranulating mast cells(8). Since there are diverse histamine-releasing agents, the identification of a common prosthetic group among them would help clarify one of the mechanisms involved. Ovomucoid, OVO, a potent histamine releaser in the rat, is chemically related to both ESM and BSG by a similar carbohydrate complex. According to Stacey(9) these substances, neutroglucoproteins or mucoproteins, are protein-carbohydrate compounds composed of a relatively high protein content and a carbohydrate complex. The carbohydrate moiety of both OVO and ESM consists of D-mannose, D-galactose, and N-acetyl-d-glucosamine while BSG differs only by containing un-

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