pulmonary surfactants

george galea.

General Considerations And Definitions.

Pulmonary alveoli of mammals are lined by by a single layer of epithelial cells forming the alveolar wall. The continuity of the cells which rest on a basement membrane, is interrupted occasionally by pores of Kohn. The alveolar wall contains two types of cells:

1) attenuated cells that are extremely thin (0.1-0.7u). These are the TYPE I cells known also known as the Surface Epithelial cells or Membrane Pneumocytes.

2) large round cells (7-14u). These are known as TYPE II cells or Great Alveolar cells or Granular Pneumocytes. (Figure 1).

On one side of the alveolar wall is the interstitium of the alveolar septum containing capillaries, lymphatics and connective tissue and on the other side between the wall and the alveolar air is the acellular 'Alveolar Lining Layer'. It covers and is somewhat adherent to the alveolar wall. It is a complex mixtures of lipids, proteins and carbohydrates and is termed the 'Surfactant System Of the Lung'. The highly surface active components of this system play an essential role in determining the normal mechanical properties of the lung, as first suggested by VON NEERGAARD (1929). They are indispensible to normal pulmonary function and may be altered either primarily or secondarily in certain pathological conditions.

Histochemistry.

Histo-chemical studies have identified some of the chemicals components of the lining. Their reactions with fluorochrome dyes show that they consist of lipids and mucins. They stain positively with Acid haematin, Alcian blue and Hales colloidal iron stain. Therefore it was concluded that pulmonary surfactants consist of a mixture of phospholipids, acid polysaccharides and mucopolysaccharides. Their reaction with phosphomolybdic acid showed that there are lipids which contain choline.

Origin.

The site of origin of the surfactant system is still very controversial. KLAUS et al (1961), have suggested that the surface active materials are secreted by the Type II cell. This theory has also been put forward by BUCKINGHAM et al. (1962), who are demonstrated using C^{14} that palmitate was concentrated in the great alveolar cells. There are in these cells spiral bodies known as Lamellar Osmiophilic Bodies (LOPB's) and they are thought to be secretory granules. Other investigators show evidence that surfactant originates in the LOPBs themselves. Klaus et al. (1961) think that these bodies are transformed mitochondria, because under experimental conditions of stress, many of the Type II cells transform into spiral bodies.

NIDEN (1967) has pointed out that vacuoles in the Type II cells could represent ingested surfactant, which has been synthesised elsewhere. He showed that these cells are phagocytic, although the process is slow and remarkably selective. CORRIN (1969) has found lytic enzymes (eg., phosphatidic acid phosphatase) in the same location, and this could well be taken to support Niden's view that Type II pneumocytes are concerned with the disposal rather than the synthesis of surfactant. However proposers of the theory, that pulmonary surfactant is secreted by the Type II cell, argue that these lytic enzymes may in fact, contribute to a synthetic process, because these may break chips of a larger molecule. So much so, that ABRAMS (1966) is of the opinion that the surface active phospholipids are part of a lipoprotein molecule. According to Niden, the Clara cells (terminal cells in the smaller bronchioles) are the secretory cells. Corrin (1969) has modified his theory and postulated that both Type II cells and the Clara cells are sites of surfactant secretion.

Chemistry.

The surfactant system, is as already indicated above, a complex mixture of lipids including neutral and phospho-lipids. These lipids may be associated with carbohydrates including, glucose, galactosamine, fucose, and other monomers. Any association between lipids and proteins in the surfactant system appears to be a loose one. Chemicals studies by Klaus et al. (1961) have confirmed that surfactants include: phosphatidyl cholines (choline phosphoglycerides); phosphatidyl ethanolamines (ethanolmine phosphoglycerides); sphingomyelins; phosphatidyl inositols and lysophosphatides.

KING and CLEMENTS, (1972) isolated 4 fractions of surface active materials from dogs' lungs extracts, using differential and density gradient centrifugation. They studied their chemical composition and their results are shown in Table 1.

TABLE 1

Composition Of Surface Active Material (% Of Dry Weight)

	Protein	Lipid	Sugars	Nitrogen	Phosphorus	Nucleic Acid
Fraction	11	81	≯ 1.5	3	3	≯ 0.5

(Modified from King and Clements: American Journal Of Physiology: 1972)

As can be readily observed all fractions are composed of lipids and protein and contain less than 2% sugars. The 4-formed fractions differed from each other in protein content but did not differ significantly in lipid composition.

Biosynthesis.

Phospholipids are synthesised rapidly in the lung. In fact, it has been demonstrated that recovering (using C^{14}) occurs within 2-4 minutes Of the phospholipids synthesised in the lung only phosphatidyl cholines' metabolism has been studied in detail. 3 main pathways are thought to be involved:

(a) the incorporation of a diglyceride and CDP (cytosine diphospho) choline to yield a phosphatidyl choline.

(b) 3 step methylation of a phosphatidyl ethanolamine.

(c) the acylation of a lysophosphatidyl choline.. A scheme of phospholipid biosynthetic pathways in the lung is shown in figure 2. SALISBURY-MURPHY and other co-workers (1969) showed that rabbit lung slices oxidized glucose to glycerol and fatty acid moeities of glycerides. The major plasma fatty acid is palmitic acid and it has been found out that dipalmitoyl phosphatidyl choline is the major component of the surfactant system. Experiments worked out by SALISBURY et al. (1969) show that plasma palmitate did not effect oxidation of glucose but increased its incorporation into glycerol moeity of the glycerides and inhibited lipogenesis from glucose.

Lipid metabolism in the lung differs in several respects from that of other tissues such as liver and adipose tissue. As already indicated, the mitochondria are thought to actively synthesise lipids, which is a task most efficiently performed by microsomes and supernatant fluid in adipose tissue and in liver.

Turnover.

Of interest are certain observations that the turnover rate of phospholipids in the alveolar lining is different from that in the pulmomary parenchyma although both are extremely rapid. It has also been postulated that transmethylation of a phosphatidyl ethanolamine to a phosphatidyl choline may take place in the lining directly.

By specific activity studies, i.e. using radioactive precursors and measuring the ratio of radioactivity to quantity of the compounds concerned TIERNEY, CLEMENTSand TRAHAN (1967) showed evidence of more than one pool of dipalmitoyl phosphatidyl choline (or dipalmitoyl lecithin-DPL).

The postulated that:

(a) there could be a a slow entry of precursors from other minor metabolic pathways within the lung itself,

(b) there could be a slow entry into the lung from other tissues e.g. muscle. It has been shown conclusievly that DPL exists in many other organs besides lung,

(c) there could be multiple pools of surface active material and these are secreted at different rates e.g. 2 cell types may secrete DPL at different rates,

(d) it could be possible that not all DPL is incorporated into surface active material. One fraction of newly syntesised DPL with a short half-life may supply DPL to the surface and the remaining portion may be incorporated into structures such as membranes and have a longer half-life.

Physical Properties.

Isolated fractions of surface active material should have physical and chemical properties consistent with the behaviour of alveolar surfaces. KING and CLEMENTS (1972) from very accurate experiments in vitro, with substances they themselves isolated, brought into light some of the physical properties of alveolar surface active molecules:

(a) it is thought that surfactant exists in 2 functionaily different components; an outer layer composed of densely packed phospholipids and an inner layer containing phospholipids in a different phsico-chemical configuration probably linked to proteins.

(b) the material isolated in vitro was capable of lowering the surface-tension of a sub-phase (constituted of approximately the ionic composition of ECF) to less than 10dyn cm^{-1} when spread on the surface in quantities that approximate those of duplex films of lipid and protein. (A duplex film in this context is defined as a film in which the lipid portion of the surface active material is at the the air interphase as a monomolecolar layer with a protein portion adsorbed beneath it).

(c) the amount of material that was recovered was sufficient in quantity to cover the alveolar surface with at least one duplex film of lipid and protein.

(d) the compressiblity of a surface film of surface active material measured at 10-15 dyn cm^{-1} surface tension was less than 0.09 cm dyn^{-1} at 37°C.

(e) surface active material adsorbed on an air-liquid interface at a rate comparable to those observed in physiological studies.

(f) surface active, material, as compared to whole lung, was enriched in dipalmitoyl phosphatidyl choline (0.5mg/gm).

Certain remarks could be made out of these physical properties. The marked lowering of surface tension is due probably to, the packing of molecules into a close -ordered array at an interphase Phospholipids are amphiphilic and arrange themselves in aqueous solution in a manner that minimizes contact between their hydrophobic portions (esterified fatty acids) and water. The minimum free energy configuartion accomplishing this objective is a large myelinic aggregate in which the hydrophobic portions of the molecule are in a non-polar environment while the polar portions (glycerol backbone and esterified alcohol) are exposed to the aqueous phase (figure 3).

The fact that it can adsorb readily on adequate surfaces fits in with current thinking, which suggests that a reservour of surface active materials exists in the alveolar subphase which can readily be absorbed to the alveolar surface as needed.

PHYSIOLOGICAL SIGNIFICANCE OF THE SURFACTANT SYSTEM.

(A) Pulmonary Mechanics and Alveolar Stability.

3 factors help to stabilize an alveolus:

(a) tissue forces,

(b) geometrical stability,

(c) changes in the lung surface tension with change in alveolar area (surface elastance)

From experiments with lung extracts of pulmonary tissue demonstrated that surface tension varies directly with area and approaches 0 at very small areas.

When a normal lung is inflated from the degassed state or from the liquid-filled state an interphase is established between the oncoming air and the material present in the airways and lung units. The pressure required to open the terminal units is related to surface tension developed at this interphase according to the Laplace relationship $P=2T/r$ where,

P is the pressure tending to resist inflation or produce collapse,

T is the surface tension at the interphase,

r is the radius of the terminal units.

At the tension found in the ECF i.e. 50 dyn cm $^{-1}$ in a surface with a radius of only 0.05mm, the pressure exerted against the air in the alveplus would be quite high (20cm of H_2O). As figures 4 indicates, the behaviour of surfactant shows a hysteresis pattern. In an expanded airspace the layer of surface active agent is attenuated and the surface tension is increased accordingly. The increase in tension is partly offset however by the increase in the radius of the airspace. As the interspace contracts to perhaps one-half its expanded size. the increasing amount of surfactant now available, reduces the surface tension, and so the pressure in the airspace is decreased.

The concentration of surfactant in the interface of tissue fluid and air at small and large alveoli is different. This is because areas of greater curvature produce the greatest suction force. This brings about a homogenuos distribution of pressure. Thus by varying the elastance, surfactant ensures that the smaller alveoli do not collapse, especially at low lung volume.

The inter-relationships of surface forces and the mechanical properties of the lung can be summarised by their contribution to volume-pressure hysteresis. (figure 5). During inflation, of the air-filled lung there is a critical opening pressure below which no air enters the lungs. This is a function of the size of the alveoli and the tension at the alveolar surface. The lung then inflates with only a small increase in pressure. There is an increase in the total number of alveoli showing an increase in volume, as well as in the size of those already open. The largest alveoli will open first. The pressure increase is also influenced by tissue elasticity. During deflation the alveoli remain open over a much larger volume range than during inflation. The greater the number of alveoli sharing a given volume, the smaller will be the retractive force developed by the lungs. All pressures during inflation therefore exceed those during defation. CLEMENTS (1973) suggested that 'surface-area/tension' hysteresis contributed to this 'volume-pressure' hysteressis by extending the volume range over which the airspaces would remain stable during deflation, as well as by producing hysteresis of individual airspaces

(B) Alveodar-Liquid Balance.

There are various forces which influence the circulation of liquid at the alveolar-capillary level. Air pressure within the alveoli and the colloid osmotic pressures tend to move liquid out of the alveolar spaces. Capillary hydrostatic pressure and intra-thoracic pressure tend to move liquid out of the capillaries. (figures 6) The lymphatic system plays a role in maintaining liquid equilibrum by draining liquid from interestices. Surface tension, plays an important role here as well. It produces a suction force which is transmitted to the alveolar wall.

If surface tension is similar to that of plasma (50 dyn cm^{-1}) there would be a net pressure differential of approximately 20mmHg. favouring transudation, when considering all pressures affecting movement. However, if surface tension were negligible, the balance of forces would favour alveolar 'dryness' during most of exhalation as surface tension approaches O. This however would favour transudation into the alveoli during most if inhalation, as surface tension increases to a maximum (approximately 40 dyn cm^{-1}). However certain investigators are of the opinion, that surface tension increases between breathing cycles from the mimimum value obtained at the end of exhalation to an intermediate or equilibrium value that is well below maximum.

(C) Pulmonary Capillary Flow.

The possibility that the suction effect produced by alveolar surface tension might reduce pericapillary pressure, and thus effect capillary blood flow has been tested by BRUDERMAN, PAIN and WEST, (1967) They indicate that the higher the surface tension, the lower the perfusion pressure required to support pulmonary flow. Thus the air-inflated lung with presumably the highest surface tension requires smaller perfusion pressures, than does the air deflated lung (lower surface tension) and the latter requires less pressure than the liquid filling lung, surface tension being virtually absent. Surfactant also affects regional blood distribution in the lung. Capillary perfusion in the superior portions of the lung is enhanced during inhalation when surface tension is highest. In effect, surface tension counteracts to some extent the opposition to flow due to gravity.

(D) Clearance Of The Alveolar Surface.

Surfactant molecules at the air-alveolar lining interphases tend to move in the plane of the surface from areas of low surface tension to areas of high tension. Such spreading may provide a clearance mechanism for the removal of extraneous material, like cellular debris or foreign particles, from the alveoli, and for the distribution of surfactant among alveoli.

(E) **Reaction To Infection.**

SHIFRINE and GOULRAY (1965) produced antibodies, to Mycoplasma mycoides, a micro-organism that causes contagious bovine pleuropneumonia and demonstrated that the antiserum preciptated both phenol extracted carbohydrate from M. mycoides and pneumogalactan, a polysaccharide from bovine lungs. Animals infected with contagious bovine pleuropneumonia produce antibodies which react with pneumogalactan and the carbohydrate from M.mycoides. The cross-reactivity indicates that the carbohydrate polymers have common linkages. The authors suggested that pneumogalactan may play a role in the pathogenesis of bovine pleuropneuomia, possibly by localising the organisms in the lungs through an antigen-antibody reaction. SCARPELLI, CLUTTARIO and TAYLOR (1967) have postulated the presence of a galactan in the alveolar lining layer of rabbits' and dogs' lungs. If indeed a galactan is part of the surfactant system, the localisation reaction of Shifrine and Gourlay would take place at the alveolar surface. The implications of these suggestions are of major importance since the mode of infectivity of micro-organisms is poorly understood at present and since it is possible that other micro-organisms have similar antigens.

(F) **Determination Of Alveolar Configuration.**

Most investigators agree that alveoli are either round or polygonal and that surface forces play a significant role in determining this configuration. The irregularities of the cell surface appear to be filled in and smoothed out by the hypophase (the part of the lining facing the alveolar cell membrane) of the lining layer.

Foetal And Neo-natal Physiology.

By the sixteenth week of intra-uterine life lung epithelial cells although undiffrentiated, are already sythesising and secreting pulmonary surfactants.

Before the onset of breathing, Type II cells line most of the alveoli and inclusions are full and dense. This suggests that surfactant is stored in the greatest relative amount at birth. The greatest demand for it, is at this stage, because a large area of lung surface must be covered with surfactant as the animal begins breathing. After 1½ hours of breathing, most of the Type II cells inclusions disappear and the number of recognisable Type II cells is greatly diminished. These morphological changes, suggest that stored surfactant is released during the first 1½ hours of life. By 24 hours a thin non-cellular surfactant lining is present.

CLUCK et al. (1967) provides a correlation to these morphological changes, by biochemical studies. At about 1-1½ hours of life is a peak of DPL secretion, and this as can be readily seen, coincides with the maximum number of free lamellar figures seen in the alveolar spaces.

Physiological Effects Of Reduction In Lung Surfactant.

Severe reduction in lung surfactant in the living organisms occurs almost exclusively in newborn humans and animals. The lungs at birth are filled with liquid which is displaced from the airspaces during the first breath into the interstitial spaces where absorption takes place via the lymphatics and directly into the circulation. At the end of the first breath the ability of retain air in the lung during expiration and form a 'Functional Residual Capacity' (FRC), depends upon the presence of surfactant in the air-liquid interphase in the alveoli. If surfactant is deficient expulsion of air during expiration can be complete. With each successive breath the alveoli have to be reopened from the collapsed state and the removal of liquid from the lung is impeded.

Gross interference with lung function follows with development of hyaline membrane disease (idiopathic respiratory distress syndrome of the newborn). In this condition deep retractions of the chest wall are present, durng inspiration, together with cyanosis and a fast respiratory frequency. There is a total alveolar atelectasis and the dilated terminal airways are lined with eosinophilic hyaline membranes composed largely of plasma proteins and epithelial debris. NORMAND thinks that the presence of plasma proteins in airspaces, implies increased permeability of the lung lining.

Measurements of lung mechanics show that lung compliance, FRC and Total Lung Capacity (TLC) are greatly reduced while airway resistance is little affected. Pulmonary vascular resistance is raised because of pulmonary vasoconstriction probably caused by the combined effects of atelectasis, hypoxia and acidosis.

Effects Of Some Physical and Chemical Factors On Pulmonary Surfactants.

Since volatile general anaesthetics must penetrate the alveolar lining layer and come into direct contact with the surfactant system, their effects on surface tension properties of lung extracts have been studied. No abnormality of surface tension was shown following exposure to anaesthetics in normal quantities either in vivo or in vitro.

Lipids analysis reveal no quantitative difference between smokers and non smokers, but the total lipid content was several times less in smokers. MILLER et al. suggest that cigarette smoking may lower tension without affecting the rate of surfactant production. However this finding is disputed.

Alterations in oxygen tension affects pulmonary surfactant. Hypoxic hypoxia reduces the number and size of inclusion bodies in Type II cells. Hyperoxia reduces the concentration of surface active phospholipids. Inhalation of 15% carbon dioxide by guinea-pigs results in hyaline membrane formation.

Surfactant formation before birth is known to be impaired by several factors, such as, aspiration of gastro-intestinal fluids, or excessive interchange with extrapulmonary fluid as, during respiratory movements. In foetal lungs there is an appeciable amount of albumin. Its function is thought to disperse the relatively insoluble phospholipids in foetal pulmonary fluid.

Surfactant concentrations may vary by alterations in the alveolar liquid environment, alterations in pulmonary blood flow, by pulmonary infections and certain surgical purocedures.

Surface tension in pulmonary extracts in-

creases when temperature is raised to 40-42°C and it is possible that the physiological properties of surfactant are altered significant during high febrile states in vivo.

Present Status And Future Prospects.

Current investigations on animals suggest that administration of suitable drugs to the preterm foetus may accelerate lung development and permit early delivery when there are appropriate obstetrical indications.

Current work also suggests that surfactant flux is under a significant measure of nervous and humoral control. This concept has far reaching implications for the role of surfactant in adjustment of the lung to varying physiological and pathological conditions. A case in point is derived from the work of REDDING (1972), who suggests that thyroxine may be a potent regulator of lung surfactant. His investigations indicate that thyroxine administration to rabbit foetuses accelerates the appearance of osmiophilic lamellar inclusions within the Type II pneumocytes.

CONCLUSION

Although not generally appreciated, the exocrine function of the lung may be its most vital function.

ACKNOWLEDGEDMENTS.

I would like to thank Mr. Raymond Agius and Mr. Joseph Magro for their valuable encouragement and assistance. I would like to thank also Dr. Roger Ellul-Micallef M.D. Ph. D. (Edin) for reviewing this article.

REFERENCES.

1. Abrams M.E.: Isolation and Quantitative Estimation of Pulmonary Surface Active Lipoproteins. Journal of Applied Physiologly: 21-718 (1966).

2. Bruduman I. et al.: Effect of Surface Tension on Circulation in the Excised Lungs of Dogs. Journal of Applied Physiology: *19*-707 (1964).

3. Buckingham S. and Arvey M.E.: Time of Appearance of Lung Surfactant In the Foetal Lung. Nature: *193*-688 (1962).

4. Clements J.A.: Smoking And Pulmonary Surfactant. New England Journal Of Medicine: *286*-261 (1972).

5. Clements J.A.: Lung Surfactant-Present Status And Future Prospects. Proceedings Of The Royal Society Of Medicine: *66*-389 (1973).

6. Copenhauer W.M. Bunge R.P. and Bunge M.B.: Baileys Textbook Of Histology Williams and Williams. (1971).

7. Corrin B.: Phagocytic Potential Of Pulmonary Alveolar Epithelium With Particular Reference To Surfactant Metabolism. Thorax: *24*-110 (1969).

8. Finley T.N. et al.: Low Yield Of Pulmonary Surfactant In Cigarette Smokers. New England Journal Of Medicine. *286*-223 (1972).

9. Fowler. G. Law Of Laplace. New England Journal Of Medicine: *285*-1087. (1971).

10. Gluck L.: The Biochemical Development Of Surface Activity In Mammalian Lung Pediatric Research: 1-123. (1967).

11. Happlelton A.G. Fletcher F. and Wyatt I. : Abnormalities Of Lining Llipids Following Inhalation Of Quartz. Experientia: *28:* 938. (1972).

12. King R.J. and Clements J.A.: Surface Active Materials From Dogs' Lungs. (a) Method Of Isolation. (b) Composition and Physiological Correlations. (c) Thermal Analysis. American Journal Of Physiology: 223-207. (1972).

13. Klaus M.H. etal.: Alveolar Epithelial Cell Mitochondria As A Source Of A Surface Active Lung Lining. Science: *137*:750 (1961).

14. Krasno J.R. Knelson J.M. and Dalldork F.G.: Changes In The Alveolar Living With Onset Of Breathing. American Journal Of Pathology: *66*-471. (1972).

15. Kuhn: Cytochemistry Of Pulmonary Alveolar Epithelial Cells. American Journal Of Pathology: 53-809. (1968).

16. Lehninger A. Biochemistry. Worth (1972).

17. Lincoln J.R.C. Barnes N.D. Gould T. and Reynolds I.O.R.: Pulmonary Mechanics And Surfactant Measurements In Canine Lung Following Re-implantation. Thorax: 24-180 (1969).

18. Mason et al.: Synthesis Of Dipalmitoyl Lecithin By Alveolar Macrophages. Journal Of Clinical Investigation: *51*-68 (1972).

19. Mclmnot: Pulmonary Surfactants. Proceedings Of The Royal Society Of Medicine: *66*-381 (1973).

20. Mendenhall R.M. and Sun C.N.: Surface Lining Of Lung Alveoli As A Structure: Nature: *201*-713. (1964).

21. Morgan T.: Alterations In Pulmonary Surface Active During Exposure To An Increased Oxygen Tension. Journal Of Clinical Investigation: *44*-1737 (1965).

22. Niden A.H.: Bronchiolar And Large Alveolar Cell In Pulmonary Phospholipid Metabilism. Science: *158*-1323 (1967).

23. Pattle R.E. Properties, Function and Origin Of the Alveolar Lining Layer Nature: *175*-1125. (1955).

24. Pattle R.E.: Surface Lining Of The Lung. Physiological Review.: *45*-48 (1965).

25. Pattle R.E. Schock C. and Battensby J.: Some Effects Of Ansesthetic On Lung Surfactant. British Journal Of Anaesthesia. :64-1119. (1972).

26. Pearse.: Histochemistry. Churchill. (1961)..

27. Redding R.A. et al.: Tyroid Hormone Influence Upon Lung Surfactant Metabolism. Science: *175*-994 (1973).

28. Reynolds T.: Physiological Effects Of Reduction In Lung Surfatant. Proceedings Of The Royal Society Of Medicine.: *66*-288. (1973).

29. Salsbiury-Murphy S. Rubenstein D. and Beck J.C. Phospholipids Snythesis In Rabbits Lung Slices Is Accelerated By The Addition Of Palmitate To the Medium. American Journal Of Physiology: 211-988 (1966).

30. Scarpelli E.M.: Pulmonary Surfactants And Their Role In Lung Diseases. Advances In Pediatrics. :*16*-177 (1969).

31. Scarpelli E.M.: Physiology And Pathology Of Pulmonary Surfactants. Triangle p. 1,047 (1971).

32. Scarpelli. E.M. Clutario B.C. and Taylor F.A.: Preliminary Identification Of the Lung Surfactant System. Journal Of Applied Physiology. *23*-880 (1967).

33. Schaefer S. et al.: Time Coure Of Changes In Surface Tension And Morphology Of Alveolar Epithelial Cells AndCO2 Induced Hyaline Membrane Disease. Journal Of Clinical Investigation: *43*-2080 (1964).

34. Schifrine M. and Gourlay R.N.: Serological Relationships Between Galactans From Normal Bovine Lung From Mycoplasma Mycoides. Nature: 208-498 (1965).

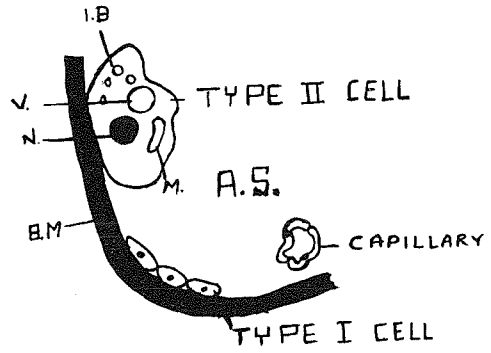
35. Tierney D.G. Clements J.A. and Trahan H.J. Rates of Replacement of Lecithins And Alveolar Instability In Rats' Lungs. American Journal 0f Physiology: *213*-671 (1967).

36. Valdivia E. et al.: Fatty Changes Of Granular Pneumocytes. Science: *151*-213 (1966).

37. Young S.L. and Tierney D.E.: Dipalmitoyl Lecithin Secretion And Metabolism In Rats' Lungs. American Journal Of Physiology: 222-1,539. (1972).

PULMONARY SURFACTANTS

FIGURE. 1

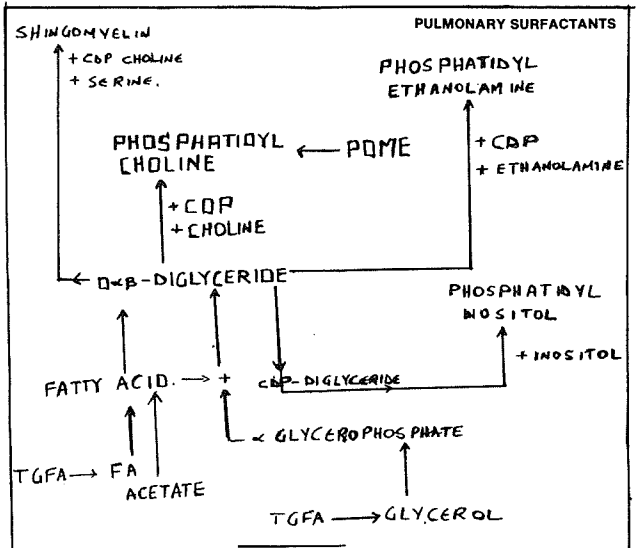


V. = VACUOLE.
I.B. = INCLUSION BODY.
N. = NUCLEUS
M. = MITOCHONDRION
B.M = BASEMENT MEMBRANE.
A.S. = ALVEOLAR SPACE.

NORMAL TYPE I AND TYPE II CELLS OF ALVEOLAR SPACE. (×8200)

(MODIFIED FROM SCARPELLI. E.M. - THE SURFACTANT SYSTEM OF THE LUNG. - 1968)

PULMONARY SURFACTANTS



(MODIFIED FROM SCARPELLI E.M.. "THE SURFACTANT SYSTEM OF THE LUNG -1968)

FIGURE 2.

PULMONARY SURFACTANTS

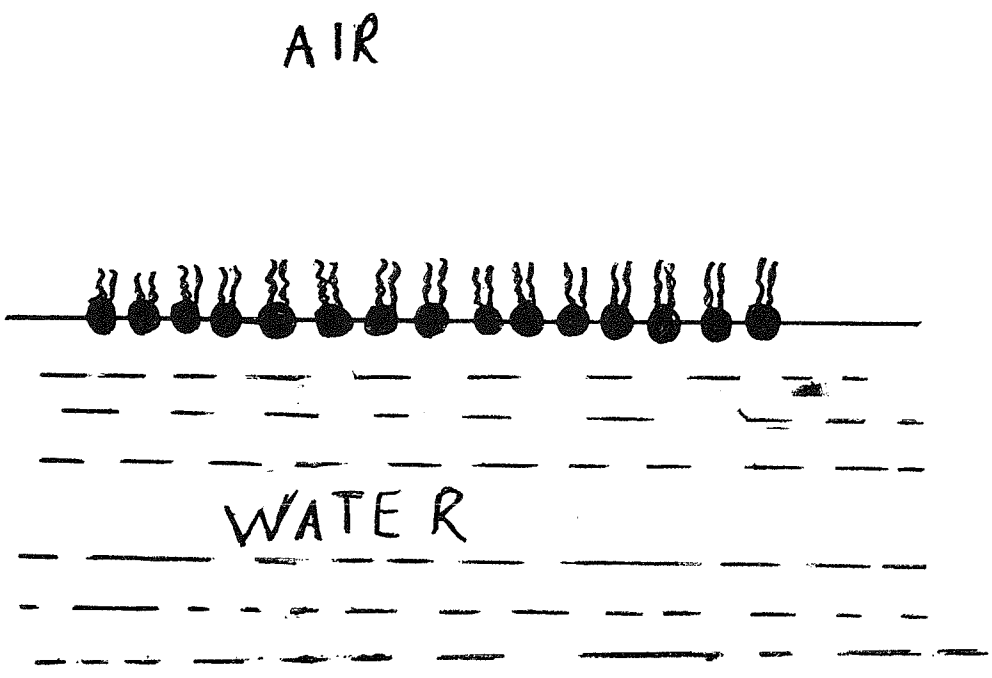
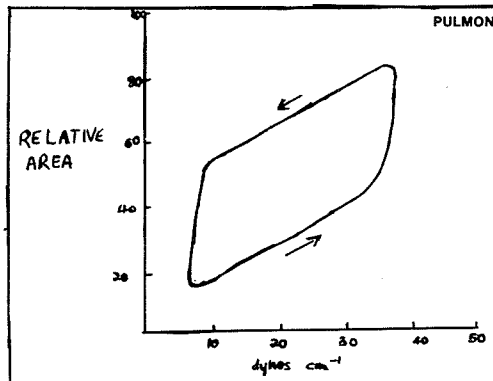
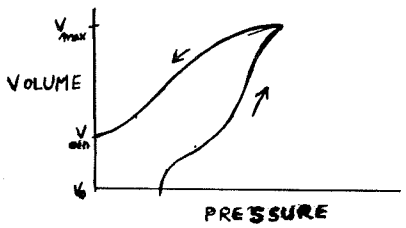


FIGURE 3



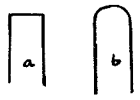


THE MAX. PRESSURE REQUIRED TO OPEN THE TERMINAL UNIT IS DETERMINED BY THE SURFACE TENSION AND THE MIN. RADIUS OF THE UNIT ONCE THE TERMINAL UNITS ARE OPENED THEY CONTINUE TO EXPAND AS INFLATION OF THE LUNG PROCEEDS. DURING DEFLATION THE LUNG CONTAINS A LARGER VOLUME OF AIR AT ANY GIVEN PRESSURE, COMPARED TO THE VOLUME IT CONTAINED DURING INFLATION. (HYSTERESIS)

FIGURE 4.

INFLATION RETRACTIVE FORCES.

1. RECRUITMENT OF INDIVIDUAL UNITS.



a. P_{min} r_{max}.
b. P_{max} r_{min}.

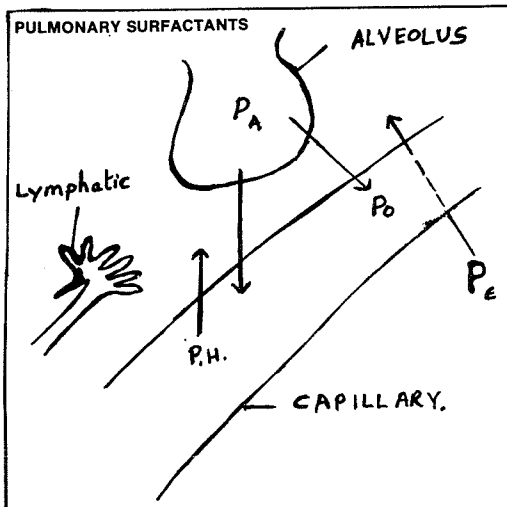
2. EXPANSION OF UNITS BEYOND HEMISHPERICAL CONFIGURATION.

3. TISSUE ELASTIC FORCES.

SKETCHES REPRESENT TERMINAL LUNG UNITS i.e. ALVEOLI AT THE END OF THE CONDUCTING UNITS (TERMINAL AIRWAYS AND DUCTS). P_{min} and P_{max} ARE THE MINIMAL AND MAXIMAL PRESSURES IN INDIVIDUAL TERMINAL UNITS. r_{min} and r_{max} ARE THE MINIMAL AND MAXIMAL RADII OF CURVATURE OF INDIVIDUAL TERMINAL UNITS.

(MODIFIED FROM SCARPELLI E.M. -THE SURFACTANT SYSTEM OF THE LUNG).

FIGURE 5



P_A - PRESSURE CAUSED BY AIR IN ALVEOLUS.

P_O - OSMOTIC PRESSURE OF PLASMA PROTEINS.

P_H - HYDROSTATIC PRESSURE WITH IN THE CAPILLARY

P_E - INTRATHORACIC PRESSURE

FIGURE 6.

CYCLIC AMP: THE UBIQUITOUS HORMONE

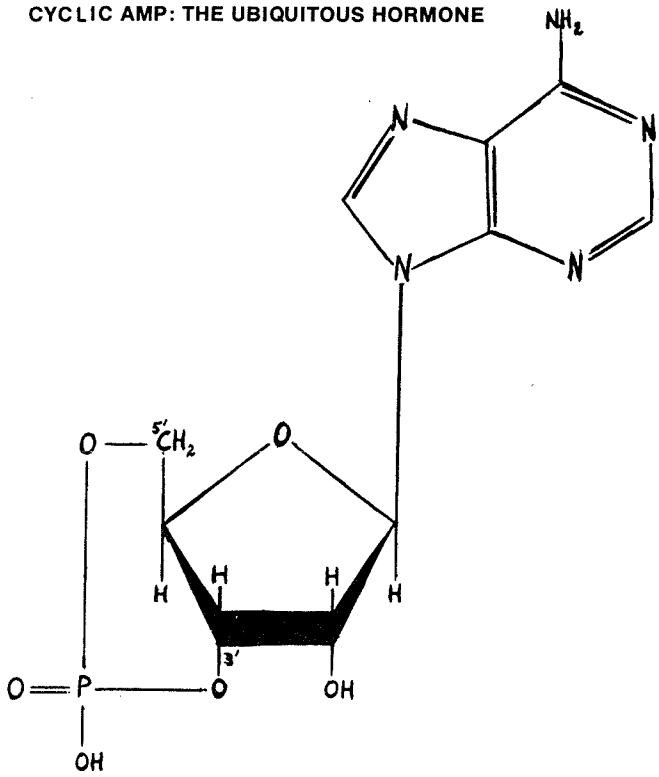


Fig. 1. Cyclic Adenosine 3',5'-Monophosphate.

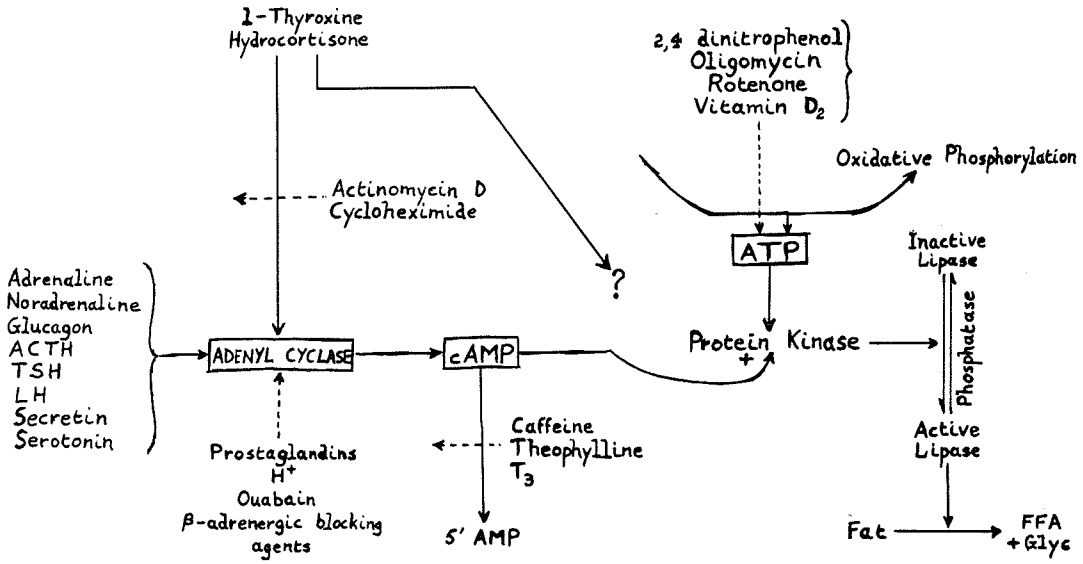


Fig. 2. Role of cAMP in lipolysis. Solid lines indicate stimulation, broken lines inhibition by cAMP. T_3 is Triiodothyronine. (Reproduced from Jost and Rickenberg: Cyclic AMP. Ann. Rev. Biochem. 40: 741-74, 1971).

CYCLIC AMP: THE UBIQUITOUS HORMONE

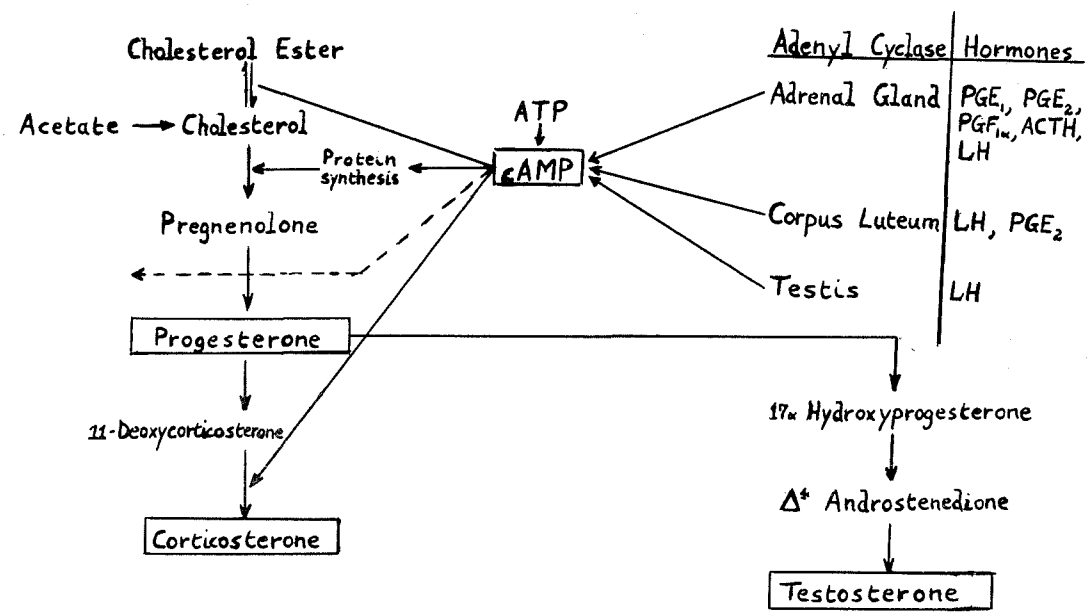


Fig. 3. Role of cAMP in Steroidogenesis. Solid lines indicate stimulation, broken lines inhibition by cAMP. (Reproduced from Jost and Rickenberg: Cyclic AMP. Ann. Rev. Biochem. 40: 741-74, 1971).

CYCLIC AMP: THE UBIQUITOUS HORMONE

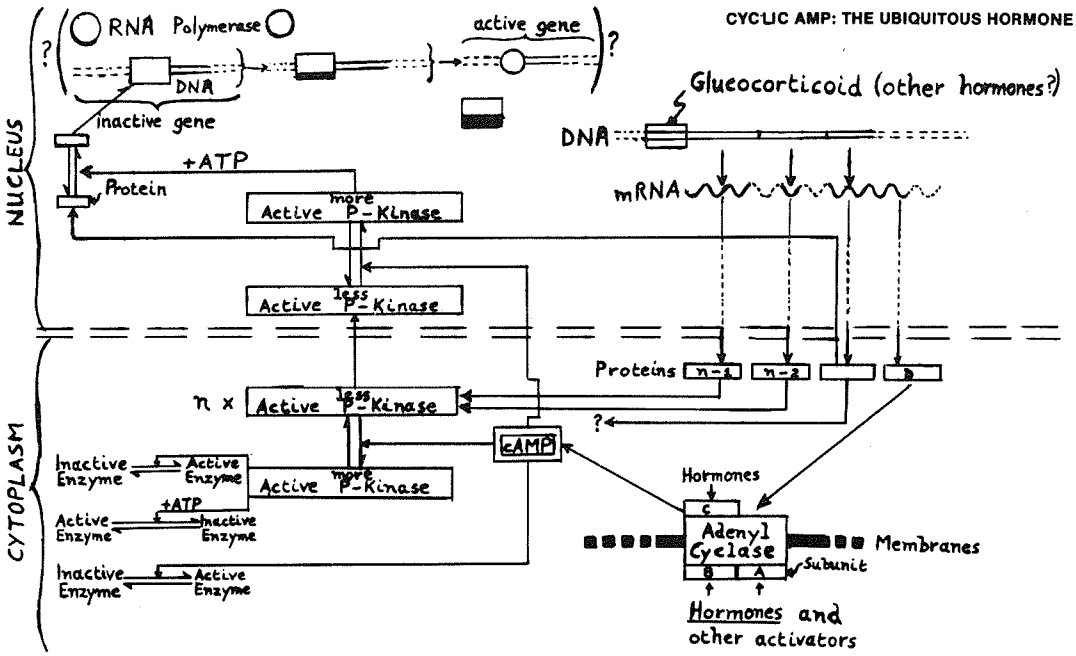


Fig. 1. The permissive (presently unexplained) effect of glucocorticoids. P-kinase denotes protein phosphokinase. (Reproduced from Jost and Rickenberg: Cyclic AMP. Ann. Rev. Biochem. 40:741-74, 1971).

A FEW FACTS ABOUT THE EBV

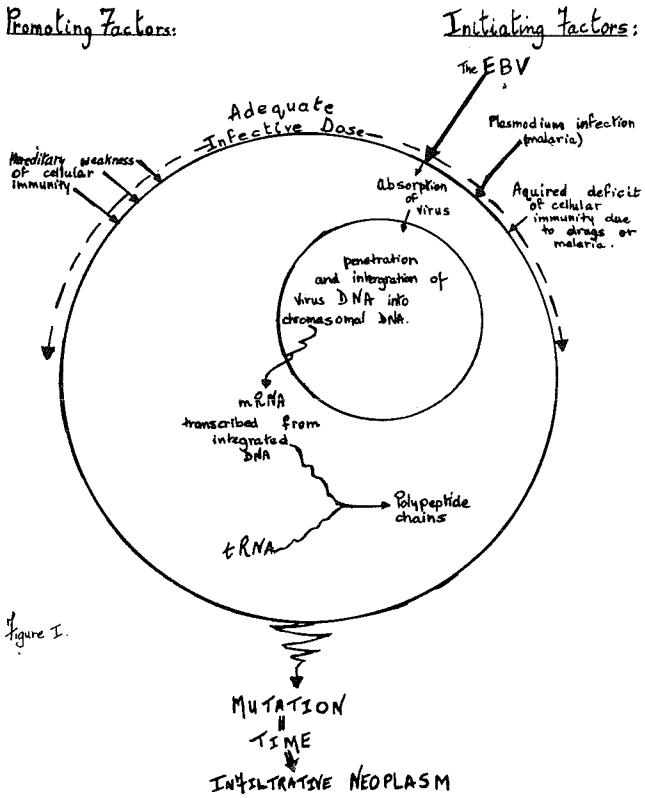
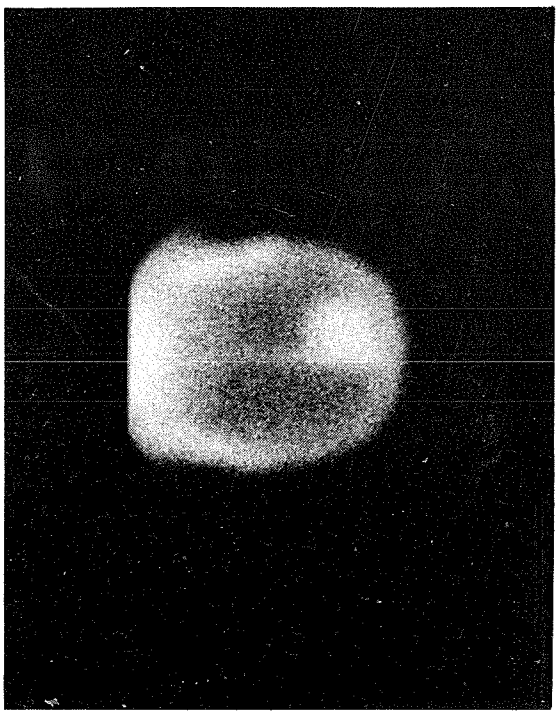


Figure I.



MENINGIOMAS