RESUSCITATION OF THE NEWBORN INFANT

A PRELIMINARY CLINICAL REPORT ON THE USE OF A DETERGENT AND A SPREADING FACTOR AS AIDS IN PULMONARY EXPANSION * †

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GRUENWALD (1) in 1947 stated that the resistance to aeration in the atelectatic lung of the newborn infant is attributable to surface tension which counteracts the entrance of air, and that surface active substances reduce the pressure necessary for aeration. Postmortem studies on atelectatic lungs of newborn infants treated with saline solution and amyl acetate before the introduction of air for expansion showed a marked reduction in pressure necessary for the introduction of air, and aeration was more diffuse than usual.

It was thought that such an observation indicated that there might be more than just surface tension which counteracts the entrance of air, and that possibly a cell cementing substance such as hyaluronic acid found normally between cells of the body may be present as an inhibitor to the expansion of some atelectatic alveoli. With the recent favorable reports of Miller (2) and Ravenel (3) on the use of a nontoxic detergent (alevaire®) in pulmonary therapy, further study is now possible on the employment of such a detergent both as a primary agent and as a vehicle for aerolization of a spreading factor such as hyaluronidase in the treatment of the atelectatic lungs of the handicapped newborn infant.

This preliminary report is based on the treatment of a group of infants showing symptoms of atelectasis and hyaline membrane disease with a nontoxic detergent (alevaire) and a spreading factor hyaluronidase (alidase®).

METHOD OF PROCESSING

The infant is placed in a nebulized fog of alevaire and alidase, using 500 units (one vial) of alidase to every 500 cc. of alevaire. The nebulized fog is produced in an air lock or incubator by a suitable nebulizer. The infant was left in the fog of alevaire and alidase until all symptoms of respiratory difficulty disappeared.

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Case Reports

Case 1. Methodist Hospital No. 22910. A female infant was delivered by cesarean section on May 14, 1953. Her birth weight was 6 pounds 9½ ounces. The stomach was lavaged at once. One and a half hours after delivery the respirations became labored and the infant cyanotic. There was a slight sternal retraction.

The mother was Rh negative and the infant Rh positive (cDE). The Coombs test was negative and the bilirubin 2 mg. The hemoglobin was 17.0 Gm., the red blood cell count 5,310,000 and no normoblasts were noted in the smear.

The infant was placed in an air lock and pressures cycled, with little improvement. Transfer was then made to an incubator provided with a nebulizer and full strength alevaire nebulized. The alevaire solution contained 500 units of alidase to every 500 cc. One hour after transfer to the incubator with nebulizer the respirations became rapid and shallow. There was some grunting. Breath sounds varied over the chest.

Six hours after delivery respirations were grunting only when the infant was disturbed. Retractions had disappeared and the color was excellent. Oxygen was continued through the night and the following morning, twenty-four hours after delivery, the infant seemed to be in excellent condition with the exception of rapid respirations. Twenty-four hours later (forty-eight hours after delivery) nebulization therapy was discontinued, the infant was removed from the incubator and was entirely normal. She remained in the hospital eight days until her mother was discharged and during this period showed no abnormal symptoms. A diagnosis of probable hyaline membrane disease of the newborn following cesarean section was made.

Case 2. Methodist Hospital No. 23790. A male infant was delivered spontaneously on May 31, 1953. His birth weight was 4 pounds 2½ ounces. Shortly after reaching the premature nursery the infant became cyanotic, and the respirations were shallow and grunting.

On physical examination four hours after delivery, respirations were rapid and the lower chest border was slightly retracted. The infant was placed in a nebulized fog of alevaire and alidase. Twelve hours later the respirations were normal, and the infant was removed from aerosol therapy twenty-four hours later. He was discharged on June 27, 1953, normal in every respect. A diagnosis of prematurity, atelectasis and possible hyaline membrane disease of the newborn was made.

Case 3. Herman Hospital No. 53–14148. A male infant was delivered by low forceps on June 6, 1953. The birth weight was 3 pounds 12½ ounces. The infant was placed in an air lock and cycling started because of mild cyanosis. Approximately one hour after delivery grunting and retraction of the chest started.

Nebulization of alevaire and alidase (500 units to 500 cc. of alevaire) was started in the air lock. The breathing improved remarkably one hour later. No grunting or retractions of the chest were noted the following day and thirty hours after delivery, the infant was removed from the air lock and placed in an incubator. He was discharged from the hospital on July 4, 1953, weighing 4 pounds 11½ ounces. A diagnosis of prematurity, and possible hyaline membrane disease of the newborn infant was made.

Case 4. Methodist Hospital No. 24991, reported through the courtesy of Dr. Mary McCaskey. This female infant was delivered on June 22, 1953, weighing

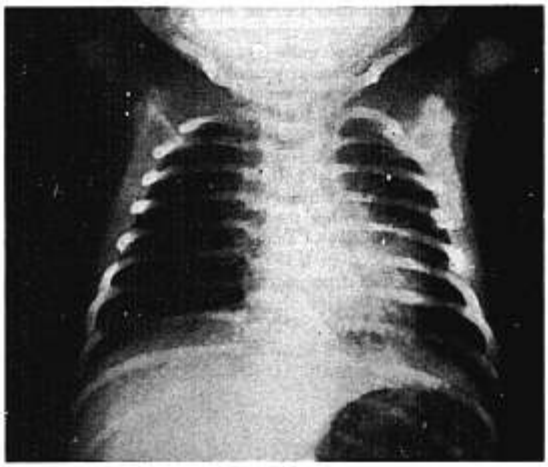

FIGURE A.

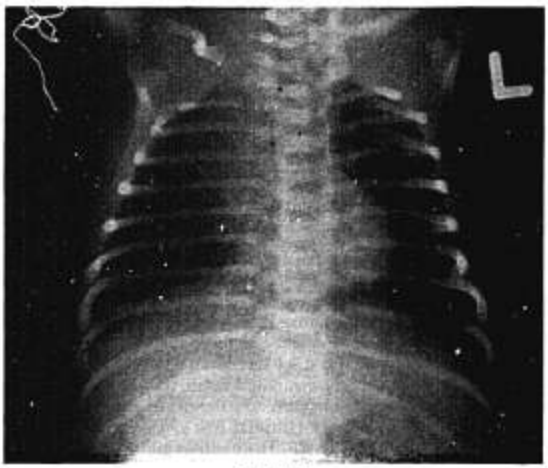

FIGURE B.

5 pounds 15 ounces. The mother had an abruptio placentae, losing about 4 pints of blood.

On delivery the infant was quite cyanotic and was placed in oxygen. Shortly after delivery the respirations became grunting and poor aeration of the left lung field noted. The cry was croupy. The hemoglobin value was 193 Gm., red blood cells numbered 5,160,000 and white blood cells 22,000. The differential count was as follows: 52 polymorphonuclear cells, 2 band forms, 40 lymphocytes, 2 monocytes and 5 eosinophils. A roentgenogram of chest, figure A, showed patchy atelectasis of both upper lungs.

The infant was placed in a nebulized fog of alevaire and alidase (500 units of alevaire). The following morning the chest sounds were improved, but still impaired. The general condition of the infant was satisfactory.

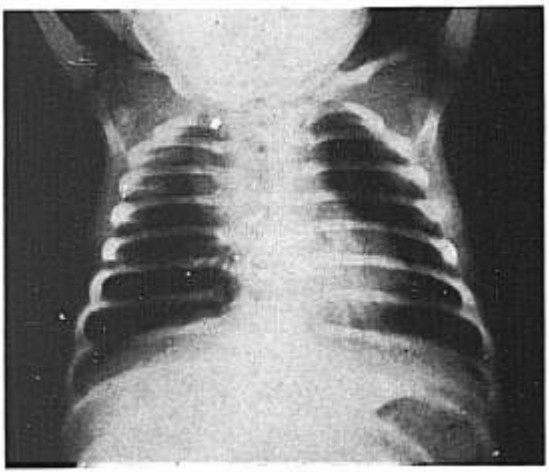

FIGURE C.

The following day the cry of the infant was almost normal, and the lungs were practically clear. On June 26, four days after delivery, the lungs were clear and nebulization of alevaire and alidase was discontinued. Roentgenographic examination on that date, figure B, showed clearing of the patchy atelectasis on the left side with some prominence of the right lobe of the thymus.

On July 6, 1953, the infant was discharged, with the chest clear. The weight was 6 pounds 1 ounce. Roentgenographic examination on that date, figure C, showed the lung fields clear with some prominence of the right lobe of the thymus.

Case 5. St. Joseph's Maternity Hospital No. 3965. A male infant was delivered by low forceps on July 4, 1953. His birth weight was 4 pounds 10 ounces. A tracheal catheter was used in resuscitation, with no results. The infant was placed in an air lock where his color improved but rapid respiration continued.

Rales were heard over both sides of the chest and there was slight retraction of the lower chest border.

Nebulization of alevaire and alidase was started in the air lock and six and a half hours later the respirations were regular. He was transferred to a standard incubator shortly afterward and progress has been normal in every respect.

A diagnosis of prematurity and atelectasis was made.

DISCUSSION

Meyer and Palmer (4) have demonstrated that there exists in the umbilical cord a free, polysaccharide acid of high molecular weight which they named hyaluronic acid. The reason for this concentration in the umbilical cord is not known. It is possible that the degree of concentration of hyaluronic acid in the umbilical cord may be an effective barrier to the expansion of the alveoli of infants after delivery by providing a strong cementing or mortar-like action of this substance between the alveolar cells of the lungs of the fetus. It is proposed now to study the cords of different newborn infants, particularly those showing difficulty in expansion, to determine whether there is any correlation between this difficulty and the content of the hyaluronic acid in the cords of such infants.

The nursing personnel have commented upon the rapidity with which the condition of infants processed in a nebulizing chamber with a detergent such as alevaire in combination with a spreading factor such as alidase becomes "good" and the infants can be transferred from such a chamber to an incubator in comparison with those processed only with a mist of water. Clinically, there appears to be quite a contrast.

A detergent such as that described by Miller (2), and later by Ravenel (3) for nebulization provides an ideal vehicle for a spreading factor such as hyaluronidase (alidase) to allow the detergent the greatest possible coverage in the atelectatic lung. The clinical results in this study bear out this possibility. Laboratory studies on the lungs of newborn infants processed with alevaire and alidase will be made and reported.

The detergent alevaire is composed of 5 per cent glycerine, 2 per cent sodium bicarbonate, and 0.125 per cent alkylarly polyether alcohol of the oxyethylate tertiary oxtylphenol-formaldehyde polymer (2). This solution has been found to be nontoxic in concentrations 250 times greater than that necessary to produce hemolysis with other detergents (5).

Hyaluronidase is a specific enzyme which hydrolyzes hyaluronic acid, a gel which serves as a cement between cells and acts as a barrier to the diffusion of invasive substances. Upon hydrolyzation of hyaluronic acid, the viscidity of this cementing gel becomes markedly lessened, resulting in a reduction of the tissue barrier which persists for approximately forty-eight hours. Theoretically, the neutralization of any barrier in the atelectatic lung of the newborn infant in order to enable that

lung to expand is a desired goal. Clinically, in the treatment of atelectasis rapid expansion occurs when a suitable detergent such as alevaire is employed in nebulization with hyaluronidase. Hyaline membrane disease of the newborn infant is favorably influenced clinically by treatment with a detergent such as alevaire in nebulization with hyaluronidase.

Questions by the Editor and Author's Replies

Query 1: What occurs when these infants are placed in an oxygen and moistened atmosphere as the only factor involved?

Answer: It is understood that this hypothetical question refers to an infant placed in mist that is generated by an efficient nebulizer such as a DeVilbiss 40. This nebulizer will generate a high percentage of mist in the particles whose radius is 1 to 3 microns so that when they leave the opening of the generator they will evaporate almost instantaneously to produce 100 per cent humidity of the air or oxygen used in the nebulizer. Assuming that the humidity of the air within the expanded portion of the infant's lungs is 100 per cent, a further breathing in of air the humidity of which also is 100 per cent will merely keep the infant's respiratory tract from becoming dry. No additional moisture will be added to the lower alveolar sacs.

Query 2: What occurs when alevaire is employed without including other measures?

Answer: When alevaire, with its constituents, glycerine, sodium bicarbonate and a detergent, is employed in an efficient nebulizer such as the DeVilbiss 40, the small particles of mist of 1 to 3 microns will reach the terminal alveolar sacs that are expanded, and the detergent, together with the sodium bicarbonate, will aid in liquefying any tenacious mucus. In addition, extra moisture in the mist will be carried to the terminal expanded alveolar sacs through the action of the glycerine.

Query 3: What occurs when alidase alone is used?

Answer: When alidase alone is used it is impossible to get the alidase into the region of the unexpanded alveolar sacs because nebulization of the particles (whose radius is 1 to 3 microns) of solution containing the alidase causes almost spontaneous evaporation. The alidase must be held in aerosol suspension with alevaire.

Query 4: If ventilation is obstructed, as it is in atelectasis, what is your conception of the mechanism by means of which the material arrives at or is provided to the region beyond the obstruction?

Answer: When alevaire and alidase are used in an efficient nebulizer, such as the DeVilbiss 40, both substances are carried to the point of obstruction in aerosol suspension. If the obstruction is mucus, liquefaction occurs as a result of the action of the detergent and sodium bicarbonate, as has been demonstrated by Miller and Boyer. If the obstruction consists of atelectatic alveoli, clinically the surface tension

holding the cells together appears to be released by the action of the alidase so that alevaire can reach the terminal portions of the lungs where liquefaction of any tenacious mucus will take place, as noted in answer to Query 2. Clinically, expansion proceeds much faster when a combination of a spreading factor and a detergent is used for relief of atelectasis.

SUMMARY

1. It is believed that in some atelectatic lungs of the newborn infant, a cell cementing substance, such as hyaluronic acid, exists. The presence of this substance may play an important part in preventing adequate and rapid progressive expansion of the alveoli after delivery in some infants.

2. A preliminary clinical report is made on the use of a detergent functioning as a primary agent, and as a vehicle for the nebulization of a spreading factor, hyaluronidase, in the treatment of atelectasis and clinical hyaline membrane disease of the newborn infant.

3. The clinical results from the use of a combination of a detergent and a spreading factor in the treatment of atelectasis and clinical hyaline membrane disease in this series warrant a further trial of this method of therapy as an aid to pulmonary expansion in the resuscitation of the newborn infant.

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