PNEUMONIA ASSOCIATED WITH BACILLUS ABORTUS (BANG) IN FETUSES AND NEW-BORN CALVES.

BY THEOBALD SMITH, M.D.

(From the Department of Animal Pathology of The Rockefeller Institute for Medical Research, Princeton, N. J.)

Plates 22 and 23.

(Received for publication, February 14, 1925.)

Lesions due to Bacillus abortus in the organs of the fetal calf have thus far received only very casual mention in the now fairly voluminous literature of infectious abortion. The generalized changes frequently present are edema of the subcutis and muscular tissue and blood-tinged effusions into the large serous cavities. These are referable to changes in the circulatory system due to partial destruction of the cotyledons. In the older fetuses, from the 7th month on, even such effusions may be absent. Some writers have described a purulent exudation into the fourth stomach. Exudates suggesting this process have been found by the writer to be exfoliated epithelium. Besides these general changes the only lesion recognizable with the naked eye in a certain number of fetuses is a consolidation of the lungs associated with a grayish mottling. It is to this pneumatic condition that the present communication is directed.

Microscopic foci made up of endothelial cells similar to those developing in inoculated guinea pigs may be found in very small numbers now in one organ, now in another in some fetuses. They are obviously of little significance beyond indicating a more general distribution of Bacillus abortus during fetal life.

A brief review of the bacteriology of this disease will serve to bring us nearer to an understanding of the pathogenesis of the pneumonia. Bacillus abortus is found in the utero-chorionic space, at first in the epithelial cells of the intercotyledonous areas, and next invading the vascular tufts of the cotyledons from the periphery. In some cases only the cotyledons are diseased. How Bacillus abortus reaches the
uterine cavity is an open question. The weight of observation suggests entrance by way of the digestive tract of the pregnant cow into the circulation and thence into the maternal and fetal cotyledons. Other routes, such as the vaginal, may come into play should the bull be diseased. A general distribution through the fetus would follow invasion of the cotyledons. Actual bacteriological studies made in this laboratory on several hundred fetuses bring to light two conditions: (a) a general distribution of *Bacillus abortus* in the organs, such as spleen, liver, kidneys, lungs, and the digestive tract; and (b) limitation of *Bacillus abortus* to the digestive tract and the lungs. In the second group the infectious agent may be considered suppressed in the organs, but multiplying or at least surviving in the contents of the stomach and intestines. Its common presence in the digestive tract and lungs in this second group is due to the fluid in which the fetus is suspended,—the amniotic fluid. The infected fetus discharges meconium into this medium and this is swallowed later by the fetus. The uniformly opalescent, clear, mucoid fluid of the stomachs in the normal fetus is converted into a thick, opaque, greenish to brownish suspension of meconium. A similar suspension is aspirated into the respiratory tract and a continuous intimate contact of the infectious agent in the meconium with the lung tissue is thus established. As a result cultures of *Bacillus abortus* are obtained from lung tissue when it is present in the digestive tract whether it is present in the internal organs or not. In view of this condition we should look first of all for lesions in the digestive tract and the lungs. Although they have not been found thus far in the former, the writer's study of this tract has not been very thorough. Macroscopic lesions are absent but the occurrence of focal microscopic lesions may be admitted. In the lungs, however, the changes in certain fetuses are evident to sight and touch, and as will be seen later, even in lungs normal in appearance certain abnormal processes are going on. The pneumonic condition established during the middle and the later fetal period may appear in the premature or full-term living calf and the infection carried in the lungs for some weeks, possibly longer.

The cases which have come under observation may be grouped into: (a) fetuses from 4 to 7 months old which have not breathed
after expulsion; (b) premature calves dying a few hours after expulsion; and (c) apparently normal calves from a few days to several weeks old in which pneumatic lesions are found when the animals are killed.

Group a.—Fetuses which have not breathed. The affected lungs are usually somewhat larger than the normal, uninfected fetal lungs. The pleural surface may be slightly irregular due to tension within the individual lobules. More characteristic is a grayish coloration involving either entire lobules or portions thereof. On section this coloration is not so clearly outlined.

The distribution of the lesions varies from case to case. In the pneumonias of young and adult bovines, the smaller cephalic and ventral lobes, as well as the azygous lobe, are involved. To this territory is frequently added the adjacent cephalic fourth or third of the main or caudal lobes. The entire diseased territories correspond with those portions of the lungs most dependent in the standing position. In the fetus no such regular distribution can be made out, although the smaller lobes appear most frequently indurated. Owing to the varying picture of the lungs from case to case the lesions are best described with reference to the fetus as a whole in a few representative cases. These are but a fraction of the fetuses studied. Unless otherwise stated, *Bacillus abortus* was isolated in pure culture from the lung tissue of all cases described, either directly or through guinea pigs, or by both methods.

No. 171.—Fetus, about 15 inches long, obtained *in utero* immediately after slaughter of the cow. Chorion presenting the typical exudate in which are demonstrable cells filled with minute bacilli. Fetus has discharged meconium abundantly into the amniotic cavity. The gross inspection of the viscera presented nothing noteworthy. Sections similarly negative except those from the lungs.

The quite universal change from the normal fetal lung is the filling up of the small bronchioles from a diameter of 0.03 mm. up with cell masses in various stages of nuclear disintegration (Fig. 1). The larger the air tube the farther advanced in this degeneration are the cells. The changes in the parenchyma are chiefly focal. The normal alveolar spacing is replaced by a more or less uniform cell infiltration filling the alveolar spaces and compressing the capillary network so that only few capillaries are in evidence. The cells are of two kinds, a fairly large cell of mononuclear type with vesicular nucleus and only little
chromatin, and a cell with a smaller, more or less densely staining nucleus. The staining is due to large blocks of chromatin. The latter cell may be either a lymphocyte or a precursor of the polynuclear cell since the chromatin may assume bizarre shapes suggesting the polymorph. In some of the smaller blood vessels (0.02 to 0.04 mm. in diameter) near or within areas of infiltration (Fig. 2), there are among the red cells large numbers of cells of the types found in the focal lesions. Elsewhere the vessels contain the normal contingent of red cells. This latter phenomenon indicates the vascular source of the cells filling the parenchyma and migrating into the air tubes. The early appearance of pneumatic lesions in this case contrasts with the absence of such lesions in a much older infected fetus, also obtained in utero, which was nearly full-term (30½ inches long).

No. 711.—Fetus, 28 inches long and weighing 23½ pounds. The usual changes such as subcutaneous edema and large amounts of meconium in stomach present. The entire lungs are permeated with whitish foci, showing distinctly subpleural and on the cut surface. These foci are 3 to 4 mm. in diameter, squarish or quadrilateral in outline, usually isolated, more rarely in groups. They are to the touch firmer than the rest of the lung tissue.

In this animal the histological changes assumed a slightly different form (Fig. 4). Besides the filling up of the smaller bronchi with cellular elements, the alveoli and alveolar passages were distended with the same type of cells. The cell moulds were permeated with a delicate network of fibrin. The lesion thus simulated a bronchopneumonia of later extrauterine life. The intensity of the infiltration varied from a bare change from the normal to a liver-like density of the cell masses.

No. 105.—Female fetus, 6 months old, hairless. Length 19¼ inches. Blood-stained effusions into serous cavities. Stomachs contain more or less fecal matter. Gross appearance of lungs normal. B. abortus found both in the digestive and pulmonary tracts and in the various organs. Sections, however, show lesions only in the lungs (Fig. 6). The smaller air tubes contain groups of cells and the normal spacing of the parenchyma has disappeared owing to its invasion by endothelial and other cells. To what extent the alveolar walls take part through infiltration with endothelial cells it is not possible to determine owing to the general similarity of the cell types of the normal tissue and the infiltrate.

No. 493.—The first pregnancy of the dam of this fetus ended normally, the second and third in abortion. In both cases B. abortus was present throughout the body. The lungs of the last fetus were pneumatic. The smaller lobes were dark red and of a liver-like consistency. A soft exudate could be pressed out of the cut air tubes. The large caudal lobes were not involved.

In sections from various regions of the affected lobes the striking feature was the filling up of all air tubes with masses of cells. The largest tube in the sections was 0.8 mm. in diameter. The central core of the cellular exudate had lost its nuclear stain, whereas the cells of the outer zones showed deeply stained nuclei. These varied much in shape, being tape-like, star-shaped, or compact. Some simulated polymorphs, but careful examination of many cells showed transition forms from.
mononuclear types. The nature of these cells remains in doubt however. The intrabronchial cell masses have their origin in the alveoli which are more or less filled with cells of the same character. These various conditions have destroyed the normal appearance of the fetal lung.

No. 270.—7 months fetus, born on pasture. Organs in general normal in appearance, excepting lungs. Only a little clear serum in peritoneal cavity. Pleural cavity contains a small amount of blood-stained fluid. Lungs airless. All the lobes of the right lung and the large caudal lobe of the left lung feel firmer than normal. Throughout these lobes there appear both subpleural and deep, grayish areas irregular in outline, but more or less rectangular, and 1 to 2 mm. in diameter. They do not project above the pleural surface and are distinguished only by their coloration. Large air tubes free from fluid or other material.

Sections indicate that the grayish foci are pneumonic. The alveoli and ultimate bronchioles are densely packed with cells of two kinds, an endothelial type and mingled with this another described under No. 171. The pneumonic infiltration is not limited to the small gray foci but in greater or less degree extends over the entire section. The gray color is due to the intensity of the process which compresses the capillary network. \textit{B. abortus} was found not only in the digestive tract and lungs but also in other organs.

\textbf{Group b.}—Expelled fetuses with partly inflated lungs.

No. 180.—Male fetus, nearly full-term, red and white, 33 inches long. Reported to have lived for 20 minutes. Lungs partially inflated. Stomachs filled with a turbid brownish fluid. Walls of fundus of fourth stomach edematous. \textit{B. abortus} was isolated from the lungs, spleen, liver, and fourth stomach.

Although the lungs appeared normal at the autopsy, sections from different lobes indicated a rather diffuse process of infiltration involving the alveolar septa and migration into the alveoli. The partial inflation had caused an irregular honeycombed condition which emphasized the broadening of the septa. Where the process was most intense, \textit{i.e.} where the parenchyma was uniformly filled up with only traces of air spaces recognizable, the small bronchioles were filled with cell debris; elsewhere they were empty.

No. 89.—Fetus born after difficult labor. It lived about an hour. Probably some days premature. Lungs only partially inflated. In the uninflated areas there are irregularly dilated spaces scattered through the collapsed regions and more or less filling up of the alveoli with cells. Cell masses in the smallest air tubes are pressed against the epithelium, probably during inspiratory efforts. \textit{B. abortus} was isolated both from placenta and lung tissue.

\textbf{Group c.}—A number of calves have been killed during the 1st week of life which were slightly premature and which showed the presence of lung lesions associated with \textit{Bacillus abortus}. 
No. 214.—Male calf, 19 days premature, 4 days old when killed. The lungs are densely sprinkled over with dark red areas of collapse from bare points to 10 mm. in diameter. Two guinea pigs inoculated with a suspension of lung tissue showed later on large spleens and _B. abortus_ was isolated therefrom. Sections of the calf's lung tissue brought out numerous cell foci in the parenchyma varying greatly in size and outline (Fig. 3). Most of them were only three to four alveoli across. They were due to the presence of endothelial cells in the alveolar walls and the lumina of alveoli. Among those in the alveoli are polymorphs. These are not found in the normal areas.

No. 218.—In another calf, 5 days old and apparently in normal condition, there was found a pale, reddish condition of the distal fifth of the right cephalic lobe. The air tube leading through this lobe was free. Sections showed an extensive broadening of the interalveolar septa with cells of endothelial type which in some lobules almost merged into complete consolidation. Polymorphs were scattered through this lobe in small numbers. Unfortunately no tests were made for _B. abortus_. Since this animal was one of a larger group of infected fetuses and calves to which the preceding calf belonged, the evidence that the lesion was due to _B. abortus_ is strong.

No. 215.—This calf was killed when 8 days old. Date of breeding not known. It was assumed to be premature but, with the exception of rapid respiration during the 1st day, it was regarded as a normal calf when killed. The lungs were extensively involved. The distal or lateral third of all the smaller lobes and the adjacent margin of both large caudal lobes are dark red, consolidated without special markings. Plugs of viscid, mucoid material in the smaller air tubes. Sections from different lobes show the same lesions. There is a general infiltration of endothelial cells so that only the bronchioles are traceable. These are filled with a mixture of mononuclears and polymorphs. The latter are found in small numbers permeating the monocytic infiltration. The pneumonic lesions of this case were at first supposed due to _B. actinoides_, although no such early case had been encountered before. In the cultures, however, there appeared in due time numerous colonies of a minute bacillus which in morphology, cultural characters, and its effect on guinea pigs was shown to be _B. abortus_.

No. 203.—This animal was 10 days old when killed. It was probably premature and the placenta diseased. In it _B. abortus_ was demonstrated in films, cultures, and inoculated guinea pigs. The calf had scourcd earlier but was apparently normal when killed. The only gross lesions found were four foci of dark red, collapsed tissue in the lungs, each 2 to 3 cm. in diameter. Cultures made directly from these foci contained miscellaneous organisms, liquefying spore bearers, moulds, and the like. Guinea pigs inoculated with suspensions of the collapsed lung developed the characteristic _B. abortus_ disease, however, and this organism was isolated from the spleens. Unfortunately material was not reserved for histological study.

---

1 Smith, T., _J. Exp. Med._, 1921, xxxiii, 441.
Besides these and other early cases, *Bacillus abortus* was encountered in several calves about a month old which were used in other experiments. In these *Bacillus abortus* was probably carried in focal lesions of the lungs.

**DISCUSSION.**

The salient characters of the fetal pneumonia associated with *Bacillus abortus* as detailed by illustrations in the preceding pages may now be briefly reviewed. The uninflated organ is firmer than normal and frequently variegated with lighter grayish areas. These may or may not be more indurated than the surrounding tissue. In the inflated lungs of the living calf foci suggesting collapse may be very small and numerous, involving all lobes or limited in numbers and causing in certain cases an airless condition of an entire lobe. The frequent occurrence of grayish foci in the fetal lungs is due to exudation into the alveoli and connecting ultimate air tubes of cell masses which crowd upon and compress the capillary network. These masses are very conspicuous in certain lungs. In others, even though *Bacillus abortus* be present, the infiltration is very slight and diffuse. These differences may be due to the varying lengths of the period of disease, as well as to the age of the fetus when the infection began.

The cell masses in the alveoli and air tubes consist of apparently two kinds of cells, the endothelial type, and another with deeply stained, round or irregularly outlined nucleus, probably a polyblast. In the air-inflated lungs, polymorphs are regularly present permeating the mass of endothelial and lymphocytic cells. The cells in the air tubes are derived from the alveolar exudate, for the epithelial layer of the plugged air tubes is intact and there is no indication of any active migration outward through the mucosa. The stimulus leading to the cellular exudate is obviously *Bacillus abortus*, brought into intimate contact with the alveolar walls through the amniotic fluid.

Fetal pneumonia affecting the living full-term or slightly premature calf may take several directions. When the uninflated territory is large, other bacteria not highly pathogenic may invade this territory and produce a rapidly fatal necrotic pneumonia. The writer encountered several peculiar cases of this kind during the height of the
epidemic when premature calves and fetuses quite regularly displayed the fetal pneumonia due to *Bacillus abortus*. One case was characterized by multiple abscesses due to staphylococci, another by widespread and numerous foci containing both staphylococci and *Aspergillus*. At that time (1918) the pneumonic lesions due to *Bacillus abortus* had not been studied and their significance as a possible groundwork for the multiplication of other bacteria not known. Hence no efforts were made to demonstrate *Bacillus abortus* in the lungs of these cases. It seems, however, justified to call attention to the possible relation of outbreaks of pneumonia in recently infected herds to the underlying *Bacillus abortus* disease even though the pneumonias are manifestly due to other organisms.

The other course probably taken by the pneumonic foci in most cases is a gradual absorption of the exudate and destruction or elimination of the infectious agent with return of the lung tissue to normal.

A diagnosis of lesions in the inflated lungs due to *Bacillus abortus* may be difficult when they are associated with other bacteria, such as *Bacillus pyogenes*, streptococci, and those mentioned above. The predominance of cells of endothelial type in suspected foci and the presence of *Bacillus abortus* as demonstrated either by direct cultures or guinea pig inoculation may be regarded as demonstrative.

The practical significance of a pneumonic condition in a fetus discharged dead is negligible. In calves born near full time it may interfere with full inflation of the lungs, favor multiplication of other pathogenic types in the uninflated regions, and simulate an outbreak of pneumonia. The failure of lungs to inflate at birth should be studied in individual cases with reference to the possible existence of a fetal pneumonia.

Pneumonic lesions due to *Bacillus abortus* may maintain the virus in the body as long as a month, according to these studies, and may perhaps account for the occasional discovery of infected unbred heifers. In such cases the bacillus may be carried to the udder and there it may survive indefinitely.

Observations made during the past 8 years upon the disease as it exists in a large herd point to the inference that fetal pneumonia, very common at the peak of the epidemic, is the result of a low resistance to the virus which is gradually raised as the epidemic subsides.
CONCLUSIONS.

A pneumonic condition in fetuses and new-born calves due to *Bacillus abortus* is pointed out for the first time, and its character, extent, and bearing on the epidemiology of pneumonia discussed.

EXPLANATION OF PLATES.

PLATE 22.

Fig. 1. Section of lung, Fetus 171 (see page 641 of text). A circumscribed pneumonic focus, surrounded by lung tissue of normal appearance, except for the cellular masses filling the bronchioles and scattering cells in the alveoli. × 86.

Fig. 2. A small vessel in the lung of the same animal, magnified 810 times in diameter to show the large proportion of mononuclear cells among the red cells (appearing as pale, granular discs in the photograph). The figure shows the two kinds of exudate cells found in the lesions, the monocyte and a cell with frequently irregularly outlined nucleus (polyblast?). About one-half of the capillaries in the sections contain the normal number of leucocytes. Those containing large numbers of leucocytes are usually associated with a focal lesion.

Fig. 3. A small focus of cells of endothelial type penetrated by polymorphs situated in inflated lung tissue from a calf 4 days old (see No.214, page 644 of the text). × 86.

PLATE 23.

Fig. 4. Lung of Fetus 711 (see page 642 of text). The cell masses filling alveoli and alveolar ducts slightly shrunken and therefore more definitely outlined. The cell masses permeated with a fine meshwork of fibrin. × 86.

Fig. 5. Uninflated normal lungs of an aborted fetus (7 months old) to show the normal fetal lungs. Although all cultures from the organs of the fetus remained sterile, the guinea pigs injected with suspensions of the uterine swab taken immediately after delivery of the fetus developed the characteristic lesions from which cultures of *B. abortus* were obtained. The various findings taken together, such as the normal condition of the viscera and the negative cultures, point to a recent infection. × 86.

Fig. 6. Lung of Fetus 105 (see page 642 of text). In this lung the bronchioles and alveolar ducts containing cell masses stand out clearly while the alveolar structure is masked by the filling up of the lumina of the alveoli with cells. × 86.
(Smith: Pneumonia associated with B. abortus.)
(Smith: Pneumonia associated with B. abortus.)